Medical Technology

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Introduction

Medical technology encompasses a wide range of healthcare products and, in one form or another, is used to diagnose, monitor or treat diseases or medical conditions affecting humans. Such technologies (applications of medical science) are intended to improve the quality of healthcare delivered and patient outcomes through earlier diagnosis, less invasive treatment options and reductions in hospital stays and rehabilitation times.

Health technology is:

Any intervention that may be used to promote health, to prevent, diagnose or treat disease or for rehabilitation or long-term care. This includes the pharmaceuticals, devices, procedures and organizational systems used in health care.

Definition

Medical technology extends and improves life. It alleviates pain, injury and handicap. Its role in healthcare is essential. Incessant medical technology innovation enhances the quality and effectiveness of care. Billions of patients worldwide depend on medical technology at home, at the doctor's, at hospital and in nursing homes. Wheelchairs, pacemakers, orthopedic shoes, spectacles and contact lenses, insulin pens, hip prostheses, condoms, oxygen masks, dental floss, MRI scanners, pregnancy tests, surgical instruments, bandages, syringes, life-support machines: more than 500,000 products (10,000 generic groups) are available today. Medical technology represents only 6,3% of total healthcare expenditure in Europe - a modest share if you consider the benefits for every member of society.
— **Eucomed**.

Allied health professions

The term **medical technology** may also refer to the duties performed by clinical laboratory professionals in various settings within the public and private sectors. The work of these professionals encompass clinical applications of chemistry, genetics, hematology, immunohematology (blood banking), immunology, microbiology, serology, urinalysis and miscellaneous body fluid analysis. These professionals may be referred to as Medical Technologists (MT) and Medical Laboratory Technologists.

Chapter 1

Assisted Reproductive Technology

Assisted reproductive technology (**ART**) is a general term referring to methods used to achieve pregnancy by artificial or partially artificial means. It is reproductive technology used primarily in infertility treatments. Some forms of *ART* are also used in fertile couples for genetic reasons. *ART* is also used in couples who are discordant for certain communicable diseases, i.e. AIDS, to reduce the risk of infection when a pregnancy is desired. The term includes any reproductive technique involving a third party e.g. a sperm donor. There is yet no strict definition of the term. Usage of the ART mainly belongs in the field of reproductive endocrinology and infertility.

Definitions

While there is no consensus on the definition, generally the process of intercourse is bypassed either by insemination (for example, artificial insemination) or fertilization of the oocytes in the laboratory environment (i.e., in vitro fertilization).

- The Centers for Disease Control and Prevention (CDC)—which is required as a result of the 1992 Fertility Clinic Success Rate and Certification Act to publish the annual ART success rates at U.S. fertility clinics—defines ART to include "all fertility treatments in which both eggs and sperm are handled. In general, ART procedures involve surgically removing eggs from a woman's ovaries, combining them with sperm in the laboratory, and returning them to the woman's body or donating them to another woman." According to CDC, "they do not include treatments in which only sperm are handled (i.e., intrauterine—or artificial—insemination) or procedures in which a woman takes medicine only to stimulate egg production without the intention of having eggs retrieved."

Procedures

Procedures are mainly fertility medication, as well as ART techniques that use more substantial and forceful interventions, of which in vitro fertilization (IVF) and expansions

of it (e.g. OCR, AZH, ICSI, ZIFT) are the most prevalent. However, there are also other manual ART, not necessarily dependent on IVF (e.g. PGD, GIFT, SSR).

Medication

Most fertility medication are agents that stimulate the development of follicles in the ovary. Examples are gonadotropins and gonadotropin releasing hormone.

In vitro fertilization

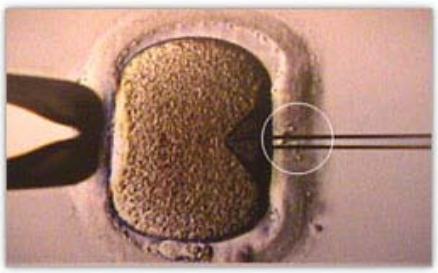
In vitro fertilization (IVF) is the technique of letting fertilization of the male and female gametes (sperm and egg) occur outside the female body.

Embryo transfer is the step in the process whereby one or several embryos are placed into the uterus of the female with the intent to establish a pregnancy.

Expansions of IVF

The following are techniques involved in, or requiring, in vitro fertilisation. In vitro fertilization does not necessarily involve each technique.

- Transvaginal ovum retrieval (OCR) is the process whereby a small needle is inserted through the back of the vagina and guided via ultrasound into the ovarian follicles to collect the fluid that contains the eggs.
- Assisted zona hatching (AZH) is performed shortly before the embryo is transferred to the uterus. A small opening is made in the outer layer surrounding the egg in order to help the embryo hatch out and aid in the implantation process of the growing embryo.



Intracytoplasmic Sperm Injection (ICSI)

Intracytoplasmic sperm injection (ICSI) is beneficial in the case of male factor infertility where sperm counts are very low or failed fertilization occurred with previous IVF attempt(s). The ICSI procedure involves a single sperm carefully

injected into the center of an egg using a microneedle. This method is also sometimes employed when donor sperm is used.

- Autologous endometrial coculture is a possible treatment for patients who have failed previous IVF attempts or who have poor embryo quality. The patient's fertilized eggs are placed on top of a layer of cells from the patient's own uterine lining, creating a more natural environment for embryo development.
- In zygote intrafallopian transfer (ZIFT), egg cells are removed from the woman's ovaries and fertilized in the laboratory; the resulting zygote is then placed into the fallopian tube.
- Cytoplasmic transfer is the technique in which the contents of a fertile egg from a donor are injected into the infertile egg of the patient along with the sperm.
- Egg donors are resources for women with no eggs due to surgery, chemotherapy, or genetic causes; or with poor egg quality, previously unsuccessful IVF cycles or advanced maternal age. In the egg donor process, eggs are retrieved from a donor's ovaries, fertilized in the laboratory with the sperm from the recipient's partner, and the resulting healthy embryos are returned to the recipient's uterus.
- A gestational carrier is an option when a patient's medical condition prevents a safe pregnancy, when a patient has ovaries but no uterus due to congenital absence or previous surgical removal, and where a patient has no ovaries and is also unable to carry a pregnancy to full term.
- Preimplantation genetic diagnosis (PGD) involves the use of genetic screening mechanisms such as Fluorescent In Situ Hybridization (FISH) or Comparative Genomic Hybridization (CGH) to help identify genetically abnormal embryos and improve healthy outcomes.
- Embryo splitting can be used for twinning to increase the number of available embryos.

Others

The following Assisted Reproduction techniques don't necessarily involve IVF.

- In gamete intrafallopian transfer (GIFT) a mixture of sperm and eggs is placed directly into a woman's fallopian tubes using laparoscopy following a transvaginal ovum retrieval.
- Sex selection is the attempt to control the sex of offspring to achieve a desired sex. It can be accomplished in several ways, both pre- and post-implantation of an embryo, as well as at birth. Pre-implantation techniques include PGD, but also sperm sorting.
- Artificial insemination (AI) is when sperm is placed into a female's uterus (intrauterine) or cervix (intracervical) using artificial means rather than by natural copulation. N.B. This can be a very low-tech process, performed at home by the woman alone or with her partner.
    - Conception devices, such as a conception cap are used to aid conception by enhancing the natural process. Conception caps are used by placing semen into a small conception cap, then placing the cap onto the cervix.

This holds the semen at the cervical os, protecting the semen from the acidic vaginal secretions and keeping it in contact with the cervical mucus.
    - Artificial insemination by donor is used in situations where the woman doesn't have a partner with functional sperm. Instead, a sperm donor supplies the sperm.
- Surrogacy, where a woman agrees to become pregnant and deliver a child for a contracted party. It may be her own genetic child, or a child conceived through in vitro fertilization or embryo transfer using another woman's ova.
- Reproductive surgery, treating e.g. fallopian tube obstruction and vas deferens obstruction, or reversing a vasectomy by a reverse vasectomy.
    - In surgical sperm retrieval (SSR) the reproductive urologist obtains sperm from the vas deferens, epididymis or directly from the testis in a short outpatient procedure.
- By cryopreservation, eggs, sperm and reproductive tissue can be preserved for later IVF.

Risks

The majority of IVF-conceived infants do not have birth defects. However, some studies have suggested that assisted reproductive technology is associated with an increased risk of birth defects. In the largest U.S. study, which used data from a statewide registry of birth defects, 6.2% of IVF-conceived children had major defects, as compared with 4.4% of naturally conceived children matched for maternal age and other factors (odds ratio, 1.3; 95% confidence interval, 1.00 to 1.67).

The main risks are:

- Genetic disorders. DNA damage increases in e.g. IVF and ICSI, which is reflected e.g. by upregulation of the gene expression of HNRNPC in the placenta.
- Low birth weight. In IVF and ICSI, a risk factor is the decreased expression of proteins in energy metabolism; Ferritin light chain and ATP5A1.
- Preterm birth. Low birth weight and preterm birth are strongly associated with many health problems, such as visual impairment and cerebral palsy, and children born after IVF are roughly twice as likely to have cerebral palsy.

Other risk factors are:

- Membrane damage, which is contributed to or reflected by increased expression of the membrane fusion proteins NAPA and Annexin A3.

Sperm donation is an exception, with a birth defect rate of almost a fifth compared to the general population. It may be explained by that sperm banks accept only people with high sperm count.

Current data indicate little or no increased risk for postpartum depression among women who use ART.

Usage

Assisted reproductive technology procedures performed in the U.S. has more than doubled since 10 years ago, with 140.000 procedures in 2006, resulting in 55.000 infants born.

In Australia, 3.1 percent of babies now born are a result of ART.

Costs

United States of America

Not everyone in the U.S. has insurance coverage for fertility investigations and treatments. Many states are starting to mandate coverage, and the rate of utilization is 277% higher in states with complete coverage.

There are some health insurance companies that cover diagnosis of infertility but frequently once diagnosed will not cover any treatment costs.

2005 approximate treatment/diagnosis costs (United States, costs in US$):

- Initial workup: hysteroscopy, hysterosalpingogram, blood tests ~$2,000
- Intrauterine Insemination (IUI) aka Artificial insemination ~ $200– 900 per. trial
- Sonohysterogram (SHG) ~ $600 – 1,000
- Clomiphene citrate cycle ~ $ 200 - 500
- IVF cycle ~ $10,000 -30,000
- Use of a surrogate mother to carry the child - dependent on arrangements

Another way to look at costs is to determine the cost of establishing a pregnancy. Thus if a clomiphene treatment has a chance to establish a pregnancy in 8% of cycles and costs $500, it will cost ~ $6,000 to establish a pregnancy, compared to an IVF cycle (cycle fecundity 40%) with a corresponding cost of ($12,000/40%) $30,000

For the community as a whole, the cost of IVF on average pays back by 700% by tax from future employment by the conceived human being.

United Kingdom

In the UK all patients have the right to preliminary testing, provided free of charge by the National Health Service. However, treatment is not widely available on the NHS and there can be long waiting lists. Many patients therefore pay for immediate treatment within the NHS or seek help from private clinics.

Sweden

In Sweden, official fertility clinics provide most necessary treatments and initial workup, but there are long waiting lists, especially for egg donations, since the donor gets just as low reward as the receiving couple are charged. However, there are private fertility clinics.

Canada

Some treatments are covered by OHIP (public health insurance) in Ontario and others are not. If you are undergoing artificial insemination or if you have bilaterally blocked fallopian tubes and are under 40, the treatment is covered but you are still required to pay lab fees which are around $3,000-4,000. Coverage would vary in other provinces. Most other patients are required to pay for treatments themselves.

Israel

Israel's National Health Insurance, which is mandatory for all Israeli citizens, covers nearly all fertility treatments. In-Vitro-Fertilization costs are fully subsidized up to the birth of two children for all Israeli women, including single women and lesbian couples. Embryo transfers for purposes of gestational surrogacy are also covered.

New Zealand

The national public health system of New Zealand covers IVF treatment in specific circumstances only, based on a 'points for conception challenges' equation. Publicly funded IVF treatments are limited (between one and three treatments dependent on criteria) and are subject to substantial wait-lists, dependent on local health funding region, which raises potential inequity of ART support across the country. Infertility testing through blood tests can be covered by public funding, however in the absence of explicit gynecological complications, additional investigations are may not be covered publicly. Investigation such as a hysterosalpingogram may be covered, but the wait-list could be in excess of six weeks, whereas a privately sourced HSG can cost $NZ900 but is readily available. Many New Zealanders select self-funded IVF cycles, at approximately $NZ10,000 per cycle, and other forms of ART, such as IUI, at approximately $NZ1200, using the services of private fertility clinics, which in itself is a growing local industry. Individuals using private services are generally not covered under personal health insurance policies in New Zealand.

Ethics

Some couples find it difficult to stop treatment despite very bad prognosis, resulting in futile therapies. This may give ART providers a difficult decision of whether to continue or refuse treatment.

Fictional representation

Films and other fiction depicting emotional struggles of assisted reproductive technology have had an upswing in the latter part of the 2000s decade, although the techniques have been available for decades. Yet, the amount of people that can relate to it by personal experience in one way or another is ever growing, and the variety of trials and struggles are huge.

Chapter 2

Computer-Aided Diagnosis

Computer-aided detection (CADe) and computer-aided diagnosis (CADx) are procedures in medicine that assist doctors in the interpretation of medical images. Imaging techniques in X-ray, MRI, and Ultrasound diagnostics yield a great deal of information, which the radiologist has to analyze and evaluate comprehensively in a short time. CAD systems help scan digital images, *e.g.* from computed tomography, for typical appearances and to highlight conspicuous sections, such as possible diseases.

CAD is a relatively young interdisciplinary technology combining elements of artificial intelligence and digital image processing with radiological image processing. A typical application is the detection of a tumor. For instance, some hospitals use CAD to support preventive medical check-ups in mammography (diagnosis of breast cancer), the detection of polyps in the colon, and lung cancer.

Overview

CADe systems are usually confined to marking conspicuous structures and sections. Computer Aided Diagnosis (CADx) systems evaluate the conspicuous structures. For example, in mammography CAD highlights micro calcification clusters and hyperdense structures in the soft tissue. This allows the radiologist to draw conclusions about the condition of the pathology. Another application is CADq, which quantifies, e.g., the size of a tumor or the tumor's behavior in contrast medium uptake. At the present stage of the technology, CAD cannot and may not substitute the doctor, but rather plays a supporting role. The doctor (generally a radiologist) is always responsible for the final interpretation of a medical image.

Computer-aided diagnosis topics

Methodology

CAD is fundamentally based on highly complex pattern recognition. X-ray images are scanned for suspicious structures. Normally a few thousand images are required to

optimize the algorithm. Digital image data are copied to a CAD server in a DICOM-format and are prepared and analyzed in several steps.

1. Preprocessing for

- Reduction of artifacts (bugs in images)
- Image noise reduction
- Leveling (harmonization) of image quality for clearing the image's different basic conditions e.g. different exposure parameter.

2. Segmentation for

- Differentiation of different structures in the image, e.g. heart, lung, ribcage , possible round lesions
- Matching with anatomic databank

3. Structure/ROI (Region of Interest) Analyze Every detected region is analyzed individually for special characteristics:

- Compactness
- Form, size and location
- Reference to close-by structures / ROIs
- Average greylevel value analyze within a ROI
- Proportion of greylevels to border of the structure inside the ROI

4. Evaluation / classification After the structure is analyzed, every ROI is evaluated individually (scoring) for the probability of a TP. Therefore the procedures are:

- Nearest-Neighbor Rule
- Minimum distance classifier
- Cascade Classifier
- Bayesian Classifier
- Multilayer perception
- Radial basis function network (RBF)
- SVM

If the detected structures have reached a certain threshold level, they are highlighted in the image for the radiologist. Depending on the CAD system these markings can be permanently or temporary saved. The latter's advantage is that only the markings which are approved by the radiologist are saved. False hits should not be saved, because an examination at a later date becomes more difficult then.

Sensitivity and specificity

CAD systems seek to highlight suspicious structures. Today's CAD systems cannot detect 100% of pathological changes. The hit rate (sensitivity) can be up to 90% depending on

system and application. A correct hit is termed a True Positive (TP), while the incorrect marking of healthy sections constitutes a False Positive (FP). The less FPs indicated, the higher the specificity is. A low specificity reduces the acceptance of the CAD system because the user has to identify all of these wrong hits. The FP-rate in lung overview examinations (CAD Chest) could be reduced to 2 per examination. In other segments (*e.g.* CT lung examinations) the FP-rate could be 25 or more.

Absolute detection rate

The absolute detection rate of the radiologist is an alternative metric to sensitivity and specificity. Overall, results of clinical trials about sensitivity, specificity, and the absolute detection rate can vary markedly. Each study result depends on its basic conditions and has to be evaluated on those terms. The following facts have a strong influence:

- Retrospective or prospective design
- Quality of the used images
- Condition of the x-ray examination
- Radiologist's experience and education
- Type of tumor
- Size of the considered tumor

Applications

CAD is used in the diagnosis of breast cancer, lung cancer, colon cancer, prostate cancer, bone metastases and coronary artery disease.

Breast cancer

CAD is used in screening mammography (X-ray examination of the female breast). Screening mammography is used for the early detection of breast cancer. CAD is especially established in US and the Netherlands and is used in addition to human evaluation, usually by a radiologist. The first CAD system for mammography was developed in a research project at the University of Chicago. Today it is commercially offered by iCAD and Hologic. There are currently some non-commercial projects being developed, such as Ashita Project, a gradient-based screening software by Alan Hshieh, as well. However, while achieving high sensitivities, CAD systems tend to have very low specificity and the benefits of using CAD remain uncertain. Some studies suggest a positive impact on mammography screening programs, but others show no improvement. A 2008 systematic review on computer-aided detection in screening mammography concluded that CAD does not have a significant effect on cancer detection rate, but does undesirably increase recall rate (*i.e.* the rate of false positives). However, it noted considerable heterogeneity in the impact on recall rate across studies.

Procedures to evaluate mammography based on magnetic resonance imaging exist too.

Lung cancer (bronchial carcinoma)

In the diagnosis of lung cancer, computed tomography with special three-dimensional CAD systems are established and considered as gold standard. At this a volumetric dataset with up to 3.000 single images is prepared and analyzed. Round lesions (lung cancer, metastases and benign changes) from 1 mm are detectable. Today all well-known vendors of medical systems offer corresponding solutions.

Early detection of lung cancer is valuable. The 5-year-survival-rate of lung cancer has stagnated in the last 30 years and is now at approximately just 15%. Lung cancer takes more victims than breast cancer, prostate cancer and colon cancer together. This is due to the asymptomatic growth of this cancer. In the majority of cases it is too late for a successful therapy if the patient develops first symptoms (*e.g.* chronic croakiness or hemoptysis). But if the lung cancer is detected early (mostly by chance), there is a survival rate at 47% according to the American Cancer Society. At the same time the standard x-ray-examination of the lung is the most frequently x-ray examination with a 50% share. Indeed the random detection of lung cancer in the early stage (stage 1) in the x-ray image is difficult. It is a fact that round lesions vary from 5–10 mm are easily overlooked. The routine application of CAD Chest Systems may help to detect small changes without initial suspicion. Philips was the first vendor to present a CAD for early detection of round lung lesions on x-ray images.

Colon cancer

CAD is available for detection of colorectal polyps in the colon. Polyps are small growths that arise from the inner lining of the Colon (anatomy). CAD detects the polyps by identifying their characteristic "bump-like" shape. To avoid excessive false positives, CAD ignores the normal colon wall, including the haustral folds. In early clinical trials, CAD helped radiologists find more polyps in the colon than they found prior to using CAD.

Coronary artery disease

CAD is available for the automatic detection of significant (causing more than 50% stenosis) coronary artery disease in coronary CT angiography (CCTA) studies. A low false positives rate (60-70% specificity per patient)) allows using CAD as a screening device distinguishing between positive and negative studies and yielding a preliminary report. This, for example, can be used for chest pain patients' triage in an emergency setting.

Nuclear medicine

CADx is available for nuclear medicine images. Commercial CADx systems for the diagnosis of bone metastases in whole-body bone scans and coronary artery disease in myocardial perfusion images exist.

Chapter 3

High-Intensity Focused Ultrasound

HIFU (**High-Intensity Focused Ultrasound**) (sometimes **FUS** or **HIFUS**) is a highly precise medical procedure using high-intensity focused ultrasound to heat and destroy pathogenic tissue rapidly. It is one modality of therapeutic ultrasound, and, although it induces hyperthermia, it should not be confused with this technique, which heats much less rapidly and to much lower therapeutic temperatures (in general < 45°C).

Clinical HIFU procedures are typically image-guided to permit treatment planning and targeting before applying a therapeutic or ablative level of ultrasound energy. When MRI is used for guidance, the technique is sometimes called **Magnetic Resonance-guided Focused Ultrasound**, often shortened to **MRgFU**. When ultrasonography is used, the technique is sometimes called **Ultrasound-guided Focused Ultrasound**, often shortened to **USgFUS**. Magnetic resonance imaging (MRI) is used to identify tumors or fibroids in the body, before they are destroyed by the ultrasound. MRgFU is currently used in Australia, the United States, Canada, Israel, Europe, and Asia to treat uterine fibroids. Ultrasonography guided HIFU is currently used in the United Kingdom, Italy, Spain, Korea, Japan, Hong Kong, Malaysia, Russia, China, Romania and Bulgaria. Current clinical trials are underway, examining the possible use of HIFU in the treatment of cancers of the brain, breast, liver, bone, and prostate.

Therapeutic ultrasound is a minimally invasive or non-invasive method to deposit acoustic energy into tissue. Applications include tissue ablation (HIFU) (for tumor treatments, for example), hyperthermia treatments (low-level heating combined with radiation or chemotherapy), or the activation or enhanced delivery of drugs.

Aiming

The ultrasound beam can be focused in these ways:

- Geometrically, for example with a lens or with a spherically curved transducer.
- Electronically, by adjusting the relative phases of elements in an array of transducers (a "phased array"). By dynamically adjusting the electronic signals to

the elements of a phased array, the beam can be steered to different locations, and aberrations due to tissue structures can be corrected.

How HIFU works

As an acoustic wave propagates through the tissue, part of it is absorbed and converted to heat. With focused beams, a very small focus can be achieved deep in tissues. When hot enough, the tissue is thermally coagulated. By focusing at more than one place or by scanning the focus, a volume can be thermally ablated. At high enough acoustic intensities, cavitation (microbubbles forming and interacting with the ultrasound field) can occur. Microbubbles produced in the field oscillate and grow (due to factors including rectified diffusion), and eventually implode (inertial or transient cavitation). During inertial cavitation, very high temperatures inside the bubbles occur, and the collapse is associated with a shock wave and jets that can mechanically damage tissue. Because the onset of cavitation and the resulting tissue damage can be unpredictable, it has generally been avoided in clinical applications. However, cavitation is currently being investigated as a means to enhance HIFU ablation and for other applications.

Method of use

In HIFU therapy, ultrasound beams are focused on diseased tissue, and due to the significant energy deposition at the focus, temperature within the tissue rises to 65° to 85°C, destroying the diseased tissue by coagulation necrosis. Each sonication of the beams treats a precisely defined portion of the targeted tissue. The entire therapeutic target is treated by moving the applicator on its robotic arm in order to juxtapose multiple shots, according to a protocol designed by the physician. This technology can achieve precise ablation of diseased tissue, therefore it is called HIFU surgery. Because it destroys the diseased tissue non-invasively, it is also known as "Non-invasive HIFU surgery". Anesthesia is not required, but should be recommended. The treatment can be combined with radiotherapy or chemotherapy.

Uses

Uterine fibroids

Development of this therapy significantly broadened the range of treatment options for patients suffering from uterine fibroids. HIFU treatment for uterine fibroids was approved by the Food and Drug Administration (FDA) in October 2004. This is a non-invasive treatment option for patients suffering from symptomatic fibroids. Most patients benefit from HIFU and symptomatic relief is sustained for two plus years. Up to 16-20% of patient will require an additional treatment .

Currently available approved uterine fibroids HIFU treatment devices are Philips Sonalleve MR-HIFU and GE Insightec ExAblate 2000 and ExAblate 2100. And CE approved Haifu model JC and JC200.

Prostate cancer

The earliest widespread use of HIFU ablation was as a treatment for prostate cancer. This treatment is administered through a trans-rectal probe and relies on heat developed by focusing ultrasound waves into the prostate to kill the tumor. Promising results approaching those of surgery have been reported in large series of prostate cancer patients. These treatments are performed under ultrasound imaging guidance, which allows for treatment planning and some minimal indication of the energy deposition. HIFU may also be used to ablate the entire prostate gland using a transrectal probe. This is an outpatient procedure that usually last 1–3 hours. Results show that it greatly reduces some of the side effects common with other treatments for prostate cancer.

During HIFU, the entire prostate is ablated, including the prostatic urethra. The urethra has regenerative ability because it is derived from a different type of tissue (bladder squamous-type epithelium) rather than prostatic tissue (glandular, fibrotic and muscular). While the urethra is an important anatomical structure, the sphincter and bladder neck are more important to maintaining the urinary function. During HIFU the sphincter and bladder neck are identified and avoided.

Available devices for prostate cancer treatment

Ablatherm Robotic HIFU

Developed in 1989 in France with Inserm (French National Institute of Medical Research), Edouard Herriot Hospital in Lyon and EDAP TMS (Nasdaq : EDAP), Ablatherm HIFU was the first prostate cancer HIFU device to receive CE marking in 2000. The first "Ablathermy" treatments on men were performed in 1993 and as of January, 2010, more than 21,000 treatments have been performed worldwide.

Sonablate 500

Developed at the early 90s for the treatment of benign prostate hyperplasia (BPH) in the US by Misonix (Nasdaq : MSON), Sonablate was then modified to treat prostate cancer at the end of the 90s. Sonablate 500 received CE marking in 2001. As of January 2010, a total of more than 9,000 treatments have been performed for benign prostate hyperplasia and over 7,000 prostate cancer treatments.

During Sonablate HIFU, the physician obtains real-time ultrasound images of the prostate and surrounding areas. From these images, a customized plan for delivering the ultrasound energy is created. The Sonablate software allows the physician to precisely define the treatment zones in order to destroy the entire gland.

Sonablate HIFU is minimally invasive, performed on an outpatient basis and typically lasts 2–4 hours, depending on the size of the prostate. There is no surgery or radiation involved. Patients wear a catheter post-procedure but are able to resume normal activities almost immediately. The Sonablate is the only HIFU device for prostate cancer that does

not require an advance surgical procedure (known as a TURP) in order to achieve effective results when treating enlarged prostate glands. Sonablate HIFU can treat large prostates up to 40 grams.

The Sonablate incorporates three-dimensional imaging to provide better visuals of the prostate, especially any irregularities, and allow the physician to create the most effective treatment plan possible. The newest technological enhancement to the Sonablate is tissue change monitoring (TCM) software, which gives real-time feedback to the physician, thus confirming if sufficient energy has been delivered to completely ablate the tissue.

Other cancers

HIFU has been successfully applied in treatment of cancer to destroy solid tumors of the bone, brain, breast, liver, pancreas, rectum, kidney, testes, prostate. At this stage cancer treatments are still in the investigatory phases as there is a need to find more about their effectiveness.

HIFU may be used to create high temperatures not necessarily to treat the cancer alone, but in conjunction with targeted delivery of cancer drugs. For example, HIFU and other devices may be used to activate temperature-sensitive liposomes, filled with cancer drug "cargo" to release the drug in high concentrations only at the tumor site(s) only where triggered to do so by the hyperthermia device. This novel approach is resulting in drug concentrations 10 times or more than traditional chemo with a fraction of the side effects since the drug is not released system-wide.

In addition, several thousand patients with different types of tumors have been treated in China with HIFU using ultrasound imaging-guided devices built by several different companies.

Delivering drugs to brain

In current research, HIFU is being used to temporarily break up the blood-brain barrier, allowing an influx of drugs into the brain. It is most effective when used in combination with an inhibitor like verapamil.

Treatment of atrial fibrillation

HIFU has been used to treat the most common heart arrhythmia, atrial fibrillation (AF). A minimally invasive catheter based system designed to ablate heart tissue responsible for propagating AF has been approved for use in Europe and is undergoing an FDA approved phase III pivotal efficacy trial in the United States.

History

The first investigations of HIFU for non-invasive ablation were reported by Lynn et al. in the early 1940s. Extensive important early work was performed in the 1950s and 1960s

by William Fry and Francis Fry at the University of Illinois and Carl Townsend, Howard White and George Gardner at the Interscience Research Institute of Champaign, Ill., culminating in clinical treatments of neurological disorders. In particular High Intensity ultrasound and ultrasound visualization was accomplished stereotaxically with a Cincinnati precision milling machine to perform accurate ablation of brain tumors. Until recently, clinical trials of HIFU for ablation were few (although significant work in hyperthermia was performed with ultrasonic heating), perhaps due to the complexity of the treatments and the difficulty of targeting the beam noninvasively. With recent advances in medical imaging and ultrasound technology, interest in HIFU ablation of tumors has increased.

The first commercial HIFU machine, called the Sonablate 200, was developed by the American company Focus Surgery, Inc. (Milipitas, CA) and launched in Europe in 1994 after receiving CE approval, bringing a first medical validation of the technology for benign prostatic hyperplasia (BPH). Comprehensive studies by practitioners at more than one site using the device demonstrated clinical efficacy for the destruction of prostatic tissue without bloodloss or long term side effects. Later studies on localized prostate cancer by Murat and colleagues at the Edouard Herriot Hospital in Lyon in 2006 showed that after treatment with the Ablatherm (EDAP TMS, Lyon, France), progression-free survival rates are very high for low- and intermediate- risk patients with recurrent prostate cancer (70% and 50% respectively) HIFU treatment of prostate cancer is currently an approved therapy in Europe, Canada, South Korea, Australia, and elsewhere. Clinical trials in the United States are expected to begin in 2006. Prostate cancer trials for the new Sonablate 500 are ongoing in the U.S.A. currently. Magnetic Resonance Guided Focused Ultrasound MRgFU was first developed by Harvey Cline and Ronald Watkins at GE Corporate R&D lab in Niskayuna NY and Kullervo Hynynen at the University of Arizona, Tucson AZ. starting in 1991. This is described in U.S. Patent #5247935.(1992) The technology was later transferred to InsighTec in Haifa Israel in 2000. The InsighTec ExAblate 2000 was the first MR Guided focused ultrasound system to obtain FDA market approval and sold commercially in the United States. Haifu Model JC and JC200 by ChongQing Haifu Ltd. are complete ultrasound guided tumor treatment systems, and they are only CE approved for beningn and malignant tumors. HIFU-2001(By Sumo Corporation Ltd) is an enhanced technology treatment system that does not require anesthesia since 2001, which are famous in Asia countries. The treatment area included Liver/Pancreas/Bladder/Uterus/Kidney.

Advantages over other techniques

High Intensity Focused Ultrasound is often considered a promising technology within the non-invasive or minimally invasive therapy segments of medical technology. HIFU's capacity to generate in-depth precise tissue necrosis using an external applicator, with no effect on the surrounding structures, is unique. The history of using therapeutic ultrasound dates back to early in the 20th century. Technology has continually improved and additional clinical applications, both diagnostic and therapeutic, have become an integral part of medicine today.

An important difference between HIFU and many other forms of focused energy, such as radiation therapy or radio surgery, is that the passage of ultrasound energy through intervening tissue has no apparent cumulative effect on that tissue.

The absence of cumulative effect of HIFU on the treated tissue means that the treatment can be repeated in case of first HIFU treatment failure or partial treatment of the prostate. As a clean treatment (= non-ionizing) HIFU is also an option to treat prostate cancer recurrence after radiation therapy failure.

Discoveries during use

Currently, the only proven imaging method to accurately quantify the heating produced during HIFU *in vivo* is Magnetic Resonance Imaging (MRI). MRI also has superior soft tissue contrast and can image in any orientation, making it the state of the art for guiding HIFU treatments. But MRI can't operate in *real-time* with HIFU, with the current state of the art being one image acquisition approximately every six seconds using a full scan of k-space. Researchers are working to reduce this image acquisition time through some of the speed enhancements common in other areas of MRI, including pulse sequences to scan a reduced k-space, constrained reconstruction, and model-based filtering using data from the bioheat equation.

Clinically, MRI-guided HIFU treatments have been tested for uterine fibroids, breast fibroadenomas, breast cancer, bone metastases, and liver tumors. The largest number of patients treated with MRI-guided HIFU have been with uterine fibroids.

USgFUS treatments have been approved with CE for wider range of benign and malignant tumors due to its higher power, precision and realtime monitoring system. The largest number of patients are uterine fibroids.

Ultrasound-guided HIFU treatments have been approved in Europe and Asia. MRI-guided treatments of uterine fibroids have been approved in Europe and Asia, and were granted FDA approval in the US in 2004.

Focal HIFU treatment

With the latest improvements in biopsy techniques enabling to better locate cancer, focal HIFU treatment (i.e. partial HIFU ablation) is now starting to be investigated to further reduce the side effects of cancer treatment.

Organizations

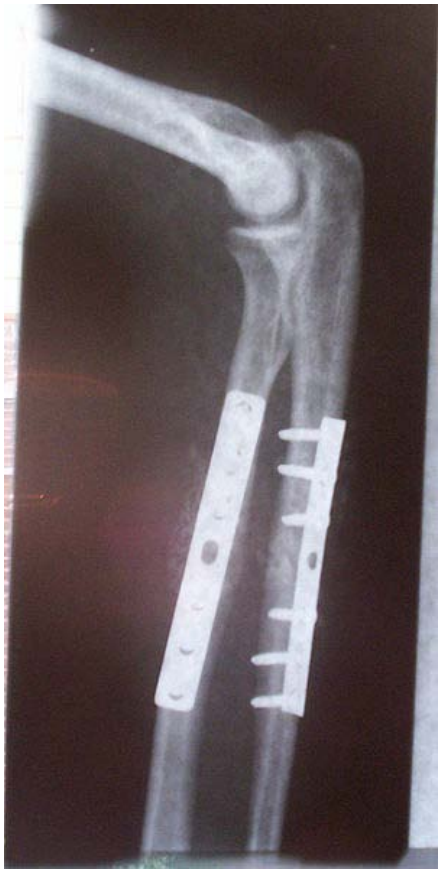
The International Society for Therapeutic Ultrasound, founded in 2001, aims to promote clinical, academic and industrial advancement in Therapeutic Ultrasound. Its primary activity is the annual International Symposium on Therapeutic Ultrasound, which has attracted experts in HIFU from throughout the world.

The Foundation for Focused Ultrasound Research is an unincorporated association promoting research into medical uses of high intensity focused ultrasound, including HIFU.

The Focused Ultrasound Surgery Foundation (**FUSF**) is working to shorten the time from technology development to patient treatment, develop new applications and accelerate the worldwide adoption of MR-guided focused ultrasound surgery

Chapter 4

Implant (Medicine)



Orthopedic implants to repair fractures to the radius and ulna. Note the visible break in the ulna. (right forearm)

An **implant** is a medical device manufactured to replace a missing biological structure, support a damaged biological structure, or enhance an existing biological structure. Medical implants are man-made devices, in contrast to a transplant, which is a transplanted biomedical tissue. The surface of implants that contact the body might be

made of a biomedical material such as titanium, silicone or apatite depending on what is the most functional. In some cases implants contain electronics e.g. artificial pacemaker and cochlear implants. Some implants are bioactive, such as subcutaneous drug delivery devices in the form of implantable pills or drug-eluting stents.

Applications

Among the most common types of medical implants are the pins, rods, screws and plates used to anchor fractured bones while they heal.

Electrically-powered implants

Active implants require electricity for their operation. Artificial pacemaker is an example of such devices that is used for treatment of Bradycardia in which the heart beats too slowly. Pacemakers can help raise the heart beat to a more normal rate through electrical stimulation of heart. Active implants could be powered up using batteries, transcutaneous energy transmission, or scavenging energy from the environment .

Bio-implants

A **bio-implant** may be defined as a biomaterial surgically implanted in a person's body to replace damaged tissue. Common areas of application include orthopedic (especially maxillofacial) re-constructive prosthesis, cardiac prostheses (artificial heart valves like the Chitra heart valve), skin and cornea.

Dental implants

Dental implants are one of the few medical devices which permanently cross the boundary between the inside and the outside of the body, since the base of the implant is osseointegrated in the bone of the mandible or maxilla and the top of the implant is in the mouth, where it can be crowned with an artificial tooth.

Orthopedic implants

In orthopedic surgery, *implants* may refer to devices that are placed over or within bones to hold a fracture reduction while *prosthesis* would be the more appropriate term for devices that replace a part or whole of a defunct joint. (In this context *implants* may be placed within or outside the body.)

Types of orthopedic implants

There are many types of orthopedic implants and each orthopedic implant is designed to correct the affected joint so that it withstands the associated movement and stress and to enhance mobility and decrease pain. Broadly speaking, Orthopedic implants are available for the hip, knee, shoulder and elbow. Safety Locking Plates

- Interlocking Nail
- Nails, Wires & Pins
- Cranio Maxillofacial Implants
- Mini Fragment Implants
- Small Fragment Implants
- Large Fragment Implants
- Cannulated Screws
- DHS/DCS & Angled Blade Plates
- Hip Prosthesis
- ACL/PCL Reconstruction System
- Spine Surgery
- External Fixators...

Complications

The process of implantation of medical devices is subject to the same complications as any other invasive medical procedure, including infection, inflammation, and pain. Implants also run the risk of rejection if they ellicit a reaction from the host immune system.

Failures

There have been many examples of implant failures, including rupture of silicone breast implants, hip replacement joints and artificial heart valves, such as the Bjork–Shiley valve, all of which have caused FDA intervention. The consequences of implant failure depend on the critical nature of the implant, and its position in the body. Thus heart valve failure is likely to threaten the life of the individual, while breast implant or hip joint failure is less likely to be life-threatening.

Chapter 5

Medical Laboratory

Clinical laboratory in a Hospital setting showing several automated analysers.

A **medical laboratory** or **clinical laboratory** is a laboratory where tests are done on clinical specimens in order to get information about the health of a patient as pertaining to the diagnosis, treatment, and prevention of disease.

Departments

Laboratory medicine is generally divided into two sections, and each of which is further divided into a number of units. These two sections are:

- Anatomic Pathology: units included here are histopathology, cytopathology, and electron microscopy. Academically, each unit is studied alone in one course. Other courses pertaining to this section include anatomy, physiology, histology, pathology, and pathophysiology.

- Clinical pathology, including :
    - Clinical Microbiology: This is the largest section in laboratory medicine; it encompasses five different sciences (units). These include bacteriology, virology, parasitology, immunology, and mycology.
    - Clinical Chemistry: Units under this busy section are instrumental analysis, enzymology, toxicology and endocrinology.
    - Hematology: This small, yet busy, section consists of two units, which are coagulation and blood bank.
    - Genetics is also studied along with a subspecialty known as cytogenetics.
    - Reproduction biology : Semen analysis, Sperm bank and assisted reproductive technology.

Distribution of clinical laboratories in health institutions varies greatly from one place to another. Take for example microbiology, some health facilities have a single laboratory for microbiology, while others have a separate lab for each unit, with nothing called a "microbiology" lab.

Laboratory equipment for hematology (black analyser) and urinalysis (left of the open centrifuge).

Here's a detailed breakdown of the responsibilities of each unit:

- Microbiology receives almost any clinical specimen, including swabs, feces, urine, blood, sputum, cerebrospinal fluid, synovial fluid, as well as possible infected tissue. The work here is mainly concerned with cultures, to look for suspected pathogens which, if found, are further identified based on biochemical tests. Also, sensitivity testing is carried out to determine whether the pathogen is sensitive or resistant to a suggested medicine. Results are reported with the identified organism(s) and the type and amount of drug(s) that should be prescribed for the patient.
- Parasitology is a microbiology unit that investigates parasites. The most frequently encountered specimen here is faeces. However, blood, urine, sputum, and other samples may also contain parasites.
- Virology is concerned with identification of viruses in specimens such as blood, urine, and cerebrospinal fluid.
- Hematology works with whole blood to do full blood counts, and blood films as well as many other specialised tests.
- Coagulation requires citrated blood samples to analyze blood clotting times and coagulation factors.

- Clinical Biochemistry usually receives serum or plasma. They test the serum for chemicals present in blood. These include a wide array of substances, such as lipids, blood sugar, enzymes, and hormones.
- Toxicology mainly tests for pharmaceutical and recreational drugs. Urine and blood samples are submitted to this lab.
- Immunology/Serology uses the concept of antigen-antibody interaction as a diagnostic tool. Compatibility of transplanted organs is also determined.
- Immunohaematology, or Blood bank determines blood groups, and performs compatibility testing on donor blood and recipients. It also prepares blood components, derivatives, and products for transfusion. Regulated by the FDA since giving blood is considered a drug, this unit determines a patient's blood type and Rh status, checks for antibodies to common antigens found on red blood cells, and cross matches units that are negative for the antigen.
- Urinalysis tests urine for many analytes. Some health care providers have a urinalysis laboratory, while others don't. Instead, each component of the urinalysis is performed at the corresponding unit. If measuring urine chemicals is required, the specimen is processed in the clinical biochemistry lab, but if cell studies are indicated, the specimen should be submitted to the cytopathology lab, and so on.
- Histopathology processes solid tissue removed from the body (biopsies) for evaluation at the microscopic level.
- Cytopathology examines smears of cells from all over the body (such as from the cervix) for evidence of inflammation, cancer, and other conditions.
- Electron microscopy prepares specimens and takes micrographs of very fine details by means of TEM and SEM.
- Genetics mainly performs DNA analysis.
- Cytogenetics involves using blood and other cells to get a karyotype. This can be helpful in prenatal diagnosis (e.g. Down's syndrome) as well as in cancer (some cancers have abnormal chromosomes).
- Surgical pathology examines organs, limbs, tumors, fetuses, and other tissues biopsied in surgery such as breast mastectomys.

Medical laboratory staff

Clinical laboratory in a Hospital setting with two technicians shown.

The following is the hierarchy of the clinical laboratory staff from highest authority to lowest:

- Medical Director
- Pathologist, Clinical biologist
- Resident in Pathology, Anatomical pathology or Clinical biology
- Pathologist Assistant,
- Laboratory Manager,
- Department Supervisor,
- Chief/Lead Technologist,
- Cytotechnologist, Medical Laboratory Scientist, Histotechnologist,
- Medical Laboratory Technician, Histotechnician
- Medical Laboratory Assistant (Lab Aide),
- Phlebotomist,
- Transcriptionist,
- Specimen processor, Secretary).

Some of these titles don't exist in some countries. Sometimes technologists and technicians do the same work. In France, clinical biologists may also be Medical director and laboratory manager.

Types of laboratory

In many countries, there are two main types of labs that process the majority of medical specimens. **Hospital laboratories** are attached to a hospital, and perform tests on patients. **Private** (or **community**) **laboratories** receive samples from general practitioners, insurance companies, and other health clinics for analysis. These can also be called reference laboratories where more unusual and obscure tests are performed. For extremely specialised tests, samples may go to a research laboratory. A lot of samples are sent between different labs for uncommon tests. It is more cost effective if a particular laboratory specializes in a rare test, receiving specimens (and money) from other labs, while sending away tests it cannot do.

In many countries there are mainly three types of Medical Laboratories as per the types of investigations carried out. 1. Clinical Pathology 2. Clinical Microbiology & 3. Clinical Biochemistry laboratories. 1. Clinical Pathology: Haematology, Histopathology, Cytology, Routine Pathology2. Clinical Microbiology: Bacteriology, Mycobacteriology, Virology, Mycology, Parasitology, Immunology, Serology.3. Clinical Biochemistry: Biochemical analysis, Hormonal assays etc.Blood Banks:- Blood bank is a separate body. Its laboratory need Microbiological analysis for infectious diseases that may be found in blood. Pathology to observe Blood grouping, Haematology & cross matching reactions. It also involves PRO department for the communication & contact for blood donations etc..

Specimen processing and work flow

Sample processing will usually start with a set of samples and a request form.

Typically a set of vacutainer tubes containing blood, or any other specimen, will arrive to the laboratory in a small plastic bag, along with the form.

The form and the specimens are given a laboratory number. The specimens will usually all receive the same number, often as a sticker that can be placed on the tubes and form. This label has a barcode that can be scanned by automated analyzers and test requests uploaded from the LIS. Entry of requests onto a laboratory management system involves typing, or scanning (where barcodes are used) in the laboratory number, and entering the patient identification, as well as any tests requested. This allows laboratory machines, computers and staff to know what tests are pending, and also gives a place (such as a hospital department, doctor or other customer) for results to go.

For biochemistry samples, blood is usually centrifuged and serum is separated. If the serum needs to go on more than one machine, it can be divided into separate tubes.

Many specimens end up in one or more sophisticated automated analysers, that process a fraction of the sample and return one or more "results". Some laboratories use robotic sample handlers (Laboratory automation) to optimize the workflow and reduce contamination risk and sample handling of the staff.

The work flow in a lab is usually heavy from 2:00 am to 10:00 am. Nurses and doctors generally have their patients tested at least once a day with general complete blood counts and chemistry profiles. These orders are then drawn during a morning run by phlebotomists for results to be available in the patient's charts for the attending physicians to consult during their morning rounds. Another busy time for the lab is after 3:00 pm when private practice physician offices are closing. Couriers will pick up specimens that have been drawn throughout the day and deliver them to the lab. Also, couriers will stop at outpatient drawing centers and pick up specimens. These specimens will be processed in the evening and overnight to ensure results will be available the following day.

Laboratory informatics

Laboratories today are held together by a system of software programs and computers that exchange data about patients, test requests, and test results known as a Laboratory information system or LIS. The LIS is interfaced with the hospital information system.

This system enables hospitals and labs to order the correct test requests for each patient, keep track of individual patient or specimen histories, and help guarantee a better quality of results as well as printing hard copies of the results for patient charts and doctors to check.

Result analysis, validation and interpretation

According to ISO 15189 norm, all pathological results must be verified by a competent professional. In some countries staff like clinical scientists do the majority of this work inside the laboratory with abnormal results referred to the relevant pathologist. In others, only medical staff (pathologist or clinical biologist) is concerned by this phase. It can be assisted by some software in order to validate normal or non modified results. Medical staff are sometimes also required in order to explain pathology results to physicians. For a simple result given by phone or for a technical problem it's a medical technologist explaining it to a registered nurse.

Departments in some countries are exclusively directed by a specialized Pathologist, in others a consultant, medical or non-medical, may be the Head of Department. Clinical Scientists have the right to interpret and discuss pathology results in their discipline in many countries, in Europe they are qualified to at least Masters level, may have a PhD and can have an exit qualification equivalent to medical staff e.g. FRCPath in the UK. In France only medical staff (Pharm.D. and M.D. specialized in Anatomical pathology or Clinical biology) can discuss pathological results, clinical scientists are not considered as a part of medical staff.

Scandal in the clinical lab industry

As medical technology advanced doctors were able to get more and more tests done in shorter and shorter amounts of time. Where in the past a doctor might order a potassium and glucose and it would take hours for the results, now a doctor can order a full chemistry panel of 20 or more different analytes and get the results in under an hour. The results are also much more accurate and reliable now than in the past. Thus, into the 1970s and 1980s the lab became a source of profit within the hospital structure.

Some commercial labs began taking illegal and nefarious actions to increase their income. These practices included Medicare and Medicaid fraud by performing and billing for tests that the ordering physician never ordered, paying kickbacks to private doctor offices for sending their specimens to these reference labs, and other complicated criminal activity. These kickbacks included donuts, free computers, fax machines, and more. These events culminated mostly in the mid-1990s with the SmithKline Beecham Clinical Laboratory (SBCL) scandal. It is believed SBCL paid at least $325 million in penalties and the industry as a whole paid over $1 billion to insurance and government agencies that were defrauded. Ever since this time, the lab has become a source of expense and loss in the hospital budget (commercial labs have nothing to do with hospitals) and lab medicine's reputation was given a black eye. Now many labs have a compliance officer with mandatory annual meetings about compliance for all employees.

Medical laboratory accreditation

Credibility of medical laboratories is paramount to the health and safety of the patients relying on the testing services provided by these labs. The international standard in use today for the accreditation of medical laboratories is ISO 15189 - Medical laboratories - particular requirements for quality and competence.

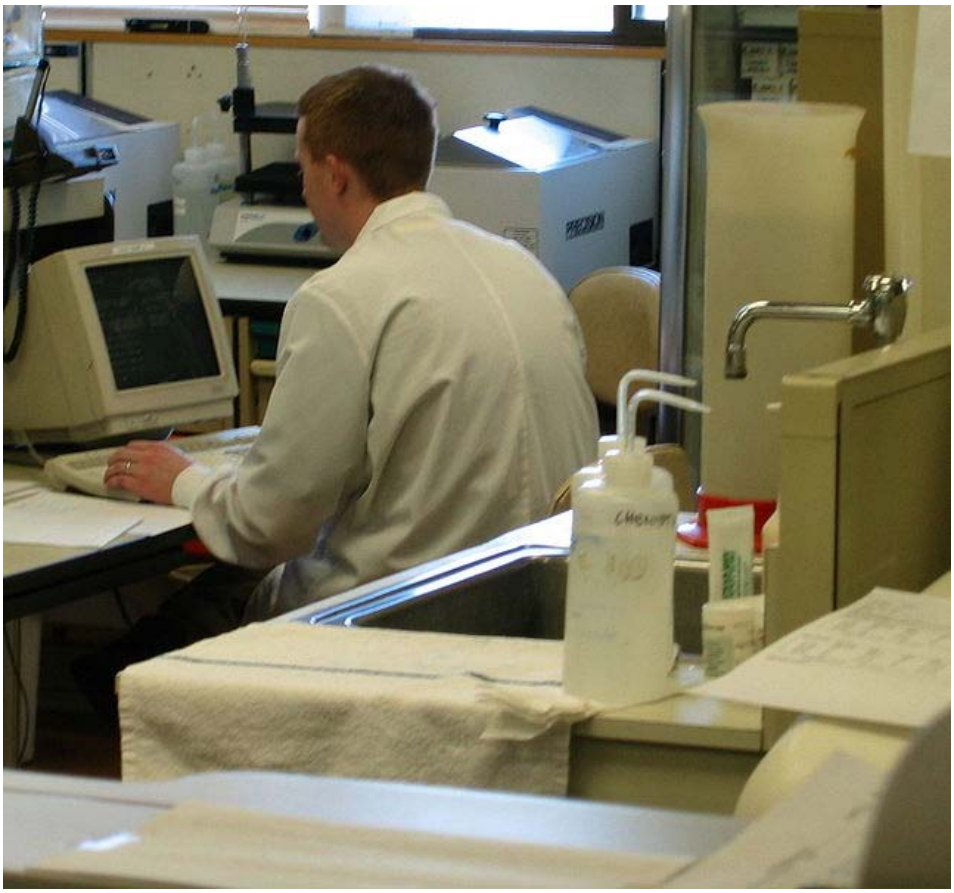
Accreditation is done by the Joint Commission, College of American Pathologists, AABB, and other state and federal agencies. CLIA 88 or the Clinical Laboratory Improvement Amendments also dictate testing and personnel.

The accrediting body in Australia is NATA, all laboratories must be NATA accredited to receive payment from Medicare.

In France, where accrediting body is COFRAC, in 2010, modification of legislation established ISO 15189 accreditation as an obligation for all clinical laboratories.

Chapter 6

Medical Laboratory Scientist



MLS in his work environment.

A **Medical Laboratory Scientist** (MLS) is a healthcare professional who performs chemical, hematological, immunologic, microscopic, and bacteriological diagnostic analyses on body fluids such as blood, urine, sputum, stool, cerebrospinal fluid (CSF), peritoneal fluid, pericardial fluid, and synovial fluid, as well as other specimens. Medical

Laboratory Scientists work in clinical laboratories at hospitals, doctor's offices, reference labs, and biotechnology labs.

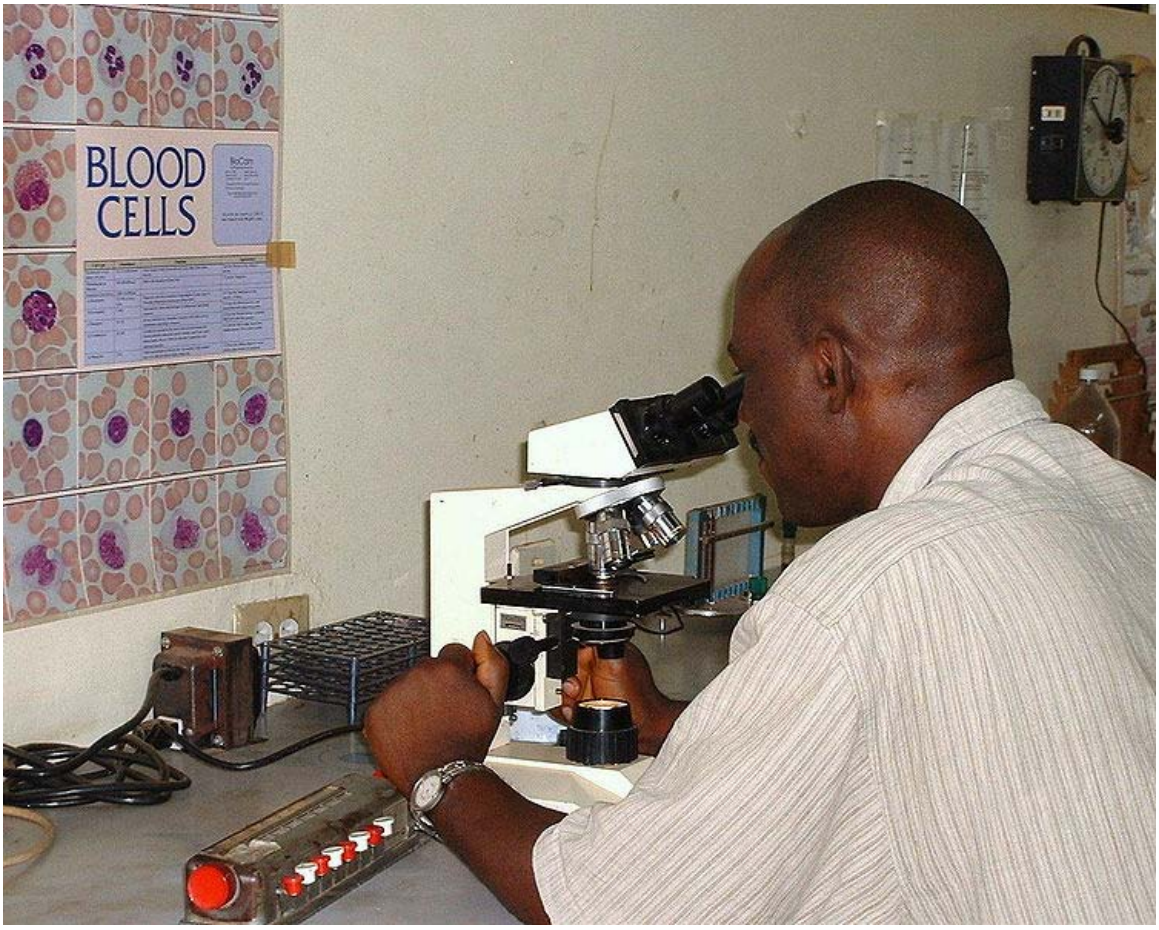
Educational requirements

A Medical Laboratory Scientist typically earns a bachelor's degree in medical laboratory science, clinical laboratory science, medical technology or in a life / biological science (biology, biochemistry, etc.) , in which case certification from an accredited training program is also required. In most four-year medical laboratory degree programs, the student attends classroom courses for three years and clinical rotations are completed in their final year of study. This combination is called a 3+1 program. There are also 2+2 programs which specialize in accepting students who have completed their lower division coursework and completing their last two years of study in the CLS program. A 4+1 program would typically be completed after a student has completed a bachelor's degree and usually takes place primarily in a clinical site rather than a college. In clinical rotations, the student experiences hands-on learning in each discipline of the laboratory and, under supervision, performs diagnostic testing in a functioning laboratory. Although not compensated, a student in the clinical phase of training usually works 40 hours per week for 20 to 52 weeks, experiencing work as a full-time employee. In addition, some universities now offer graduate level programs to allow students who have undergraduate degrees in disciplines unrelated to science to enter the field.

In the United States, a similar two-year degree qualifies the graduate to work as a medical laboratory technician (MLT). Depending on the state where employment is granted, the job duties are very similar, but MLTs receive training more exclusively in laboratory sciences. The shorter training time is attractive to many students, but there are disadvantages to this route. For example, CLSs usually earn higher salaries than MLTs, and some institutions do not employ MLTs at all.

In Canada, three-year college programs are offered that include seven semesters, two of them comprising an unpaid internship. The student graduates before taking a standard examination (such as the Canadian Society for Medical Laboratory Science, or CSMLS, exam) to be qualified as a medical laboratory technologist. Many MLTs go on to receive a bachelor of science degree after they are certified, but a few university programs affiliate with a college MLT program to allow students to graduate with both MLT certification and a degree.

Certification and licensing



MLS examining a slide.

Medical Laboratory Scientists who are certified and in good standing with the American Society for Clinical Pathology (ASCP) are entitled to use the credential "MLS" after their names. Formerly before the merger between ASCP and the National Credentialing Agency for Laboratory Personnel (NCA), Medical Laboratory Scientists certified by (ASCP) were entitled to use the credential "MT" (for Medical Technologist) and if credentialed by (NCA), the credential "CLS" (Clinical Laboratory Scientist) was used. Those certified by the Department of Health Services (HHS formally HEW), the American Association of Bioanalysts (AAB) and the American Medical Technologists (AMT) are still entitled to use the credential "MT." Additional certifying agencies include the National Healthcareer Association, National Phlebotomy Association, the National Center for Competency Testing, and the Accrediting Bureau of Health Education Schools. However the NCA and ASCP have now merged into the major certification agency.

In the United States, the Clinical Laboratory Improvement Amendments (CLIA '88) define the level of qualification required to perform tests of various complexity. Clinical Laboratory Scientists is the highest level of qualification, and CLSs are generally

qualified to perform the most complex clinical testing including HLA testing (also known as tissue typing) and blood type reference testing.

In addition to the national certification, 12 states (California, Florida, Georgia, Hawaii, Louisiana, Montana, Nevada, North Dakota, Rhode Island, Tennessee, West Virginia and New York) and Puerto Rico also require a state license. Minnesota, Texas, Illinois, Massachusetts, Michigan, Vermont, Washington, New Jersey, Iowa, Utah, Ohio, South Carolina, Wyoming, Pennsylvania, Virginia, South Dakota, Delaware, Missouri, Georgia and Alaska are currently attempting to obtain licensure. All states require documentation from a professional certification agency before issuing state certification. A person applying for state certification may also be expected to submit fingerprints, education and training records, and competency certification. Some states also require completion of a specified number of continuing education contact hours prior to issuing or renewing a license.

Some states recognize another state's license if it is equal or more stringent, but currently California does not recognize any other state license.

In the UK Medical Laboratory Scientists are known as Biomedical Scientists and must hold an honours degree from a university accredited by the Institute of Biomedical Science before they can embark upon a period of in-house training of at least 1 year before being assessed by the IBMS for state registration purposes. The title "Biomedical Scientist" is a protected title and can only be used by a person registered on the Health Professions Council register.

Specialty areas

Most Medical Laboratory Scientists are *generalists*, skilled in all areas of the clinical laboratory. However some CLSs are specialists, qualified by unique undergraduate education or additional training to perform more complex analyses than usual within a specific field. Specialties include clinical biochemistry, hematology, coagulation, microbiology, bacteriology, virology, parasitology, mycology, immunology, immunohematology (blood bank), histopathology, histocompatibility, cytopathology, genetics, cytogenetics, electron microscopy, and IVF labs. Medical Technologists specialty may use additional credentials, such as "SBB" (Specialist in Blood Banking) from the American Association of Blood Banks, or "SH" (Specialist in Hematology) from the ASCP. These additional notations may be appended to the base credential, for example, "MLS(ASCP)SBB".

Job duties

Medical Laboratory Scientists work in all areas of the clinical laboratory including blood banking, chemistry, hematology, immunology, histology and microbiology. They perform a full range of laboratory tests – from simple prenatal blood tests, to more complex tests to uncover diseases such as HIV/AIDS, diabetes, and cancer. They are also responsible for confirming the accuracy of test results, and reporting laboratory findings

to pathologists and other physicians. The information that a Medical Laboratory Scientists gives to the doctor influences the medical treatment a patient will receive. Medical Laboratory Scientists operate complex electronic equipment, computers, and precision instruments costing millions of dollars.

A Medical Laboratory Scientist analyzes human fluid samples using techniques available to the clinical laboratory, such as manual white blood cell differentials, bone marrow counts, analysis via microscopy, and advanced analytical equipment. Medical Laboratory Scientists assist doctors and nurses in choosing the correct lab tests and ensure proper collection methods. Medical Laboratory Scientists then receive the patient specimens, analyze the specimens, interpret and report results. A Pathologist may confirm a diagnostic result, but often the Medical Laboratory Scientist is responsible for interpreting and communicating critical patient results to the physician.

Medical Laboratory Scientists must recognize anomalies in their test results and know how to correct problems with the instrumentation. They monitor, screen, and troubleshoot analyzers featuring the latest technology available on the market. The MLS performs equipment validations, calibrations, quality controls, "STAT" or run-by-run assessment, statistical control of observed data, and recording normal operations. To maintain the integrity of the laboratory process, the medical laboratory scientist recognizes factors that could introduce error and rejects contaminated or sub-standard specimens.

Common tests performed by Medical Laboratory Scientists are complete blood count (CBC), comprehensive metabolic panel (CMP), electrolyte panel, liver function tests (LFT), renal function tests (RFT), thyroid function test (TFT), urinalysis, coagulation profile, lipid profile, blood type, semen analysis (for fertility and post-vasectomy studies), serological studies and routine cultures. In some facilities that have few phlebotomists, or none at all, (such as in rural areas) Medical Laboratory Scientists may perform phlebotomy on patients, as this skill is part of the clinical training.

Role in the healthcare process

A Medical Laboratory Scientist's role is to provide accurate laboratory results in a timely manner. Safeguards, such as experimental controls, calibration of laboratory instruments, delta checks (monitoring of significant changes within a normal series of results, formerly known as the "previous patients check"), and periodic surveys from the College of American Pathologists (CAP), ensure accuracy. Laboratory results aid clinical practitioners in confirming or ruling out diagnoses, monitoring chronic disease changes, and analyzing the effects of medical therapies.

Job title

The informal abbreviations of job titles may be a source of confusion. Medical Laboratory Scientist (ASCP) and Medical Technologists (AMT) or (AAB) are often called "med techs" (based on the era in which they were known as "medical technologists"), but this shorthand term is shared by other healthcare employees,

including pharmacy techs, x-ray techs and, formerly, respiratory techs, (now called respiratory therapists) and medical laboratory technicians (MLTs).

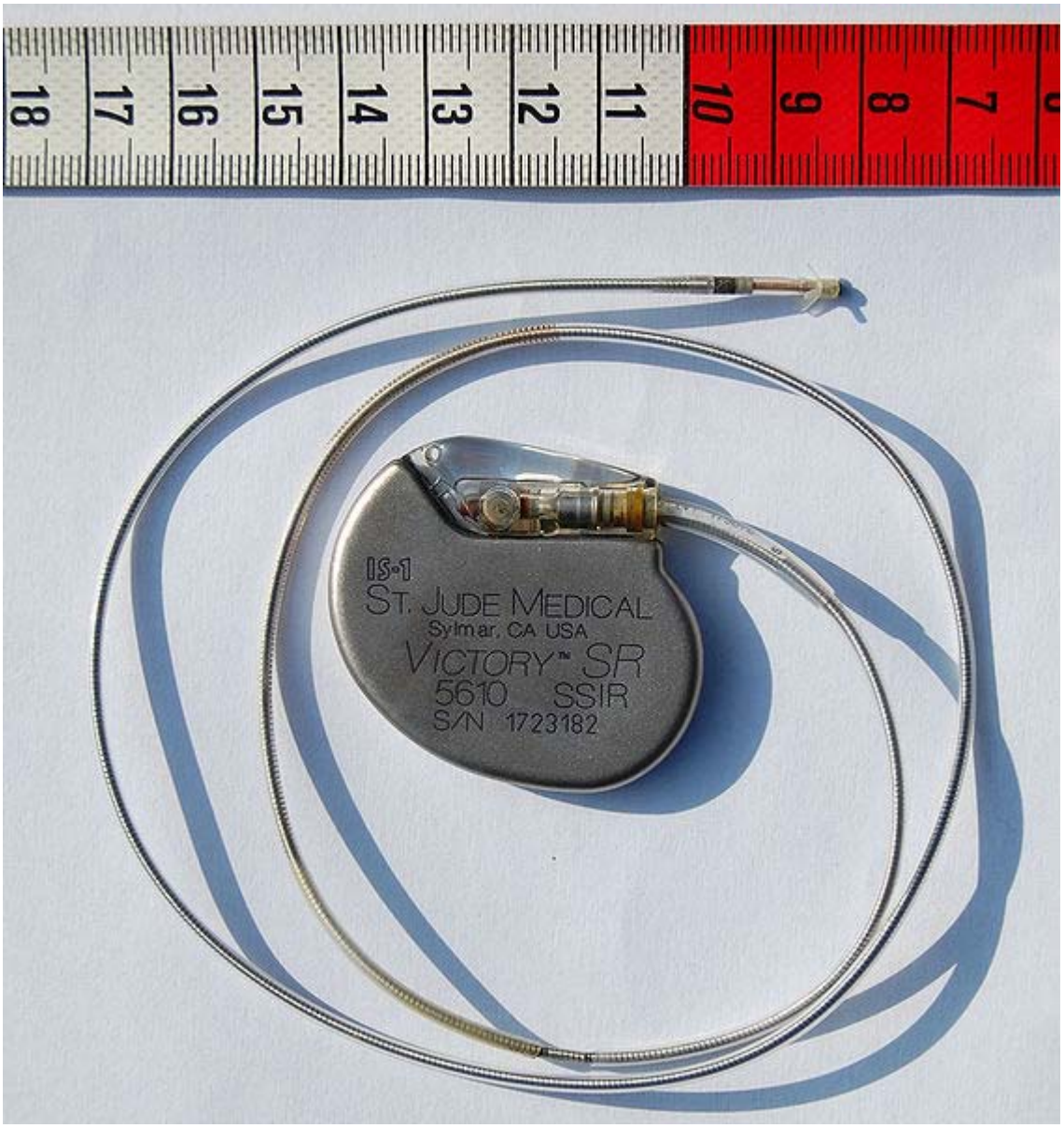
There is a formal distinction between an MLT and an MT/CLS that is not always understood by others. Both may be certified or registered by one or more nationally-recognized professional organizations, but technicians have a two-year associates degree, and may have less classroom training than other professionals. MTs and CLSs have a bachelors degree and usually do more difficult, complex analyses than technicians are trained to do. Scientists and technologists generally earn a higher income than technicians do and have more opportunities for advancement.

Much of the confusion could also be from the fact that the NCA and the ASCP certification agency, had two different titles (clinical laboratory scientist and medical technologist respectively) but with the two of them merging together into a "newer" ASCP and that organization choosing the name "Medical Laboratory Scientist", it can be said that finally the field has a "unified" title between the two organizations, however, the AMT still continues to use the title Medical Technologist.

Chapter 7

Artificial Pacemaker

A pacemaker, scale in centimeters



An artificial pacemaker with electrode for transvenous insertion (from St. Jude Medical). The body of the device is about 4 centimeters long, the electrode measures between 50 and 60 centimeters (20 to 24 inches).

A **pacemaker** (or **artificial pacemaker**, so as not to be confused with the heart's natural pacemaker) is a medical device which uses electrical impulses, delivered by electrodes contacting the heart muscles, to regulate the beating of the heart. The primary purpose of a pacemaker is to maintain an adequate heart rate, either because the heart's native pacemaker is not fast enough, or there is a block in the heart's electrical conduction system. Modern pacemakers are externally programmable and allow the cardiologist to select the optimum pacing modes for individual patients. Some combine a pacemaker and defibrillator in a single implantable device. Others have multiple electrodes stimulating

differing positions within the heart to improve synchronisation of the lower chambers of the heart.

History

The first implantable pacemaker.

In 1958, Arne Larsson (1915-2001) became the first to receive an implantable pacemaker. He had a total of 26 devices during his life and campaigned for other patients needing pacemakers.

In 1899, J A McWilliam reported in the British Medical Journal of his experiments in which application of an electrical impulse to the human heart in asystole caused a ventricular contraction and that a heart rhythm of 60-70 beats per minute could be evoked by impulses applied at spacings equal to 60-70/minute.

In 1926, Dr Mark C Lidwell of the Royal Prince Alfred Hospital of Sydney, supported by physicist Edgar H Booth of the University of Sydney, devised a portable apparatus which "plugged into a lighting point" and in which "One pole was applied to a skin pad soaked in strong salt solution" while the other pole "consisted of a needle insulated except at its point, and was plunged into the appropriate cardiac chamber". "The pacemaker rate was variable from about 80 to 120 pulses per minute, and likewise the voltage variable from

1.5 to 120 volts" In 1928, the apparatus was used to revive a stillborn infant at Crown Street Women's Hospital, Sydney whose heart continued "to beat on its own accord", "at the end of 10 minutes" of stimulation.

In 1932, American physiologist Albert Hyman, working independently, described an electro-mechanical instrument of his own, powered by a spring-wound hand-cranked motor. Hyman himself referred to his invention as an "artificial pacemaker", the term continuing in use to this day.

An apparent hiatus in publication of research conducted between the early 1930s and World War II may be attributed to the public perception of interfering with nature by 'reviving the dead'. For example, "Hyman did not publish data on the use of his pacemaker in humans because of adverse publicity, both among his fellow physicians, and due to newspaper reporting at the time. Lidwell may have been aware of this and did not proceed with his experiments in humans".

An external pacemaker was designed and built by the Canadian electrical engineer John Hopps in 1950 based upon observations by cardio-thoracic surgeon Wilfred Gordon Bigelow at Toronto General Hospital . A substantial external device using vacuum tube technology to provide transcutaneous pacing, it was somewhat crude and painful to the patient in use and, being powered from an AC wall socket, carried a potential hazard of electrocution of the patient by inducing ventricular fibrillation.

A number of innovators, including Paul Zoll, made smaller but still bulky transcutaneous pacing devices in the following years using a large rechargeable battery as the power supply.

In 1957, Dr. William L. Weirich published the results of research performed at the University of Minnesota. These studies demonstrated the restoration of heart rate, cardiac output and mean aortic pressures in animal subjects with complete heart block through the use of a myocardial electrode. This effective control of postsurgical heart block proved to be a significant contribution to decreasing mortality of open heart surgery in this time period.

The development of the silicon transistor and its first commercial availability in 1956 was the pivotal event which led to rapid development of practical cardiac pacemaking.

In 1958, engineer Earl Bakken of Minneapolis, Minnesota, produced the first wearable external pacemaker for a patient of Dr. C. Walton Lillehei. This transistorised pacemaker, housed in a small plastic box, had controls to permit adjustment of pacing heart rate and output voltage and was connected to electrode leads which passed through the skin of the patient to terminate in electrodes attached to the surface of the myocardium of the heart.

The first clinical implantation into a human of a fully implantable pacemaker was in 1958 at the Karolinska Institute in Solna, Sweden, using a pacemaker designed by Rune Elmqvist and surgeon Åke Senning, connected to electrodes attached to the myocardium

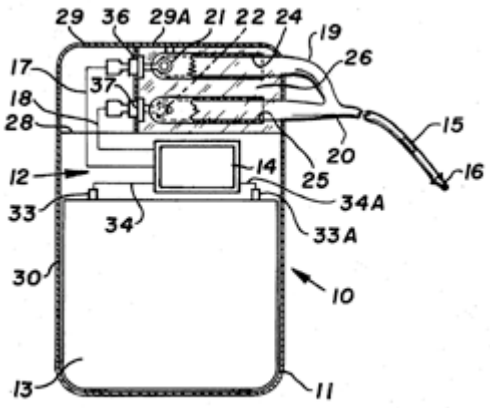
of the heart by thoracotomy. The device failed after three hours. A second device was then implanted which lasted for two days. The world's first implantable pacemaker patient, Arne Larsson, went on to receive 26 different pacemakers during his lifetime. He died in 2001, at the age of 86, outliving the inventor as well as the surgeon.

In 1959, temporary transvenous pacing was first demonstrated by Furman *et al.*. in which the catheter electrode was inserted via the patient's basilic vein.

In February 1960, an improved version of the Swedish Elmqvist design was implanted in Montevideo, Uruguay in the Casmu Hospital by Doctors Fiandra and Rubio. That device lasted until the patient died of other ailments, 9 months later. The early Swedish-designed devices used rechargeable batteries, which were charged by an induction coil from the outside.

Implantable pacemakers constructed by engineer Wilson Greatbatch entered use in humans from April 1960 following extensive animal testing. The Greatbatch innovation varied from the earlier Swedish devices in using primary cells (mercury battery) as the energy source. The first patient lived for a further 18 months.

The first use of transvenous pacing in conjunction with an implanted pacemaker was by Parsonnet in the USA, Lagergren in Sweden and Jean-Jaques Welti in France in 1962-63. The transvenous, or pervenous, procedure involved incision of a vein into which was inserted the catheter electrode lead under fluoroscopic guidance, until it was lodged within the trabeculae of the right ventricle. This method was to become the method of choice by the mid-1960s.



World's first Lithium-iodide cell powered pacemaker. Cardiac Pacemakers Inc. 1972

The preceding implantable devices all suffered from the unreliability and short lifetime of the available primary cell technology which was mainly that of the mercury battery.

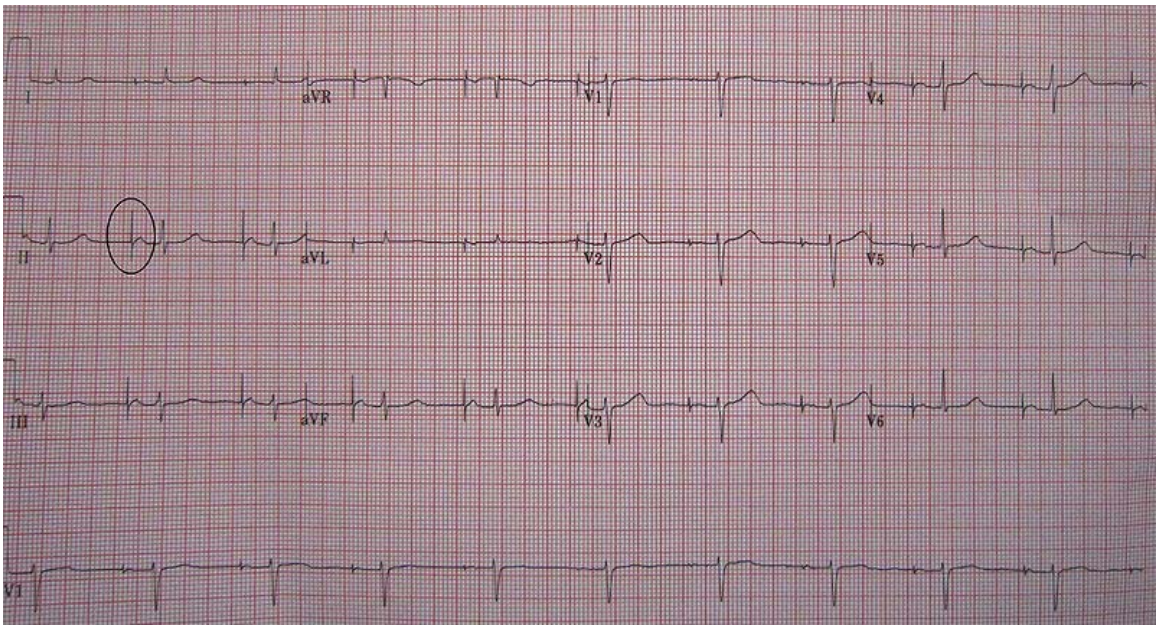
In the late 1960s, several companies, including ARCO in the USA, developed isotope powered pacemakers, but this development was overtaken by the development in 1971 of

the lithium-iodide cell by Wilson Greatbatch. Lithium-iodide or lithium anode cells became the standard for future pacemaker designs.

A further impediment to reliability of the early devices was the diffusion of water vapour from the body fluids through the epoxy resin encapsulation affecting the electronic circuitry. This phenomenon was overcome by encasing the pacemaker generator in an hermetically sealed metal case, initially by Telectronics of Australia in 1969 followed by Cardiac Pacemakers Inc of Minneapolis in 1972. This technology, using titanium as the encasing metal, became the standard by the mid-1970s.

Others who contributed significantly to the technological development of the pacemaker in the pioneering years were Bob Anderson of Medtronic Minneapolis, J.G (Geoffrey) Davies of St George's Hospital London, Barouh Berkovits and Sheldon Thaler of American Optical, Geoffrey Wickham of Telectronics Australia, Walter Keller of Cordis Corp. of Miami, Hans Thornander who joined previously mentioned Rune Elmquist of Elema-Schonander in Sweden, Janwillem van den Berg of Holland and Anthony Adducci of Cardiac Pacemakers Inc.Guidant.

Methods of pacing



An ECG in a person with an atrial pacemaker. Note the circle around one of the sharp electrical spike in the position were one would expect the P wave.

Percussive pacing

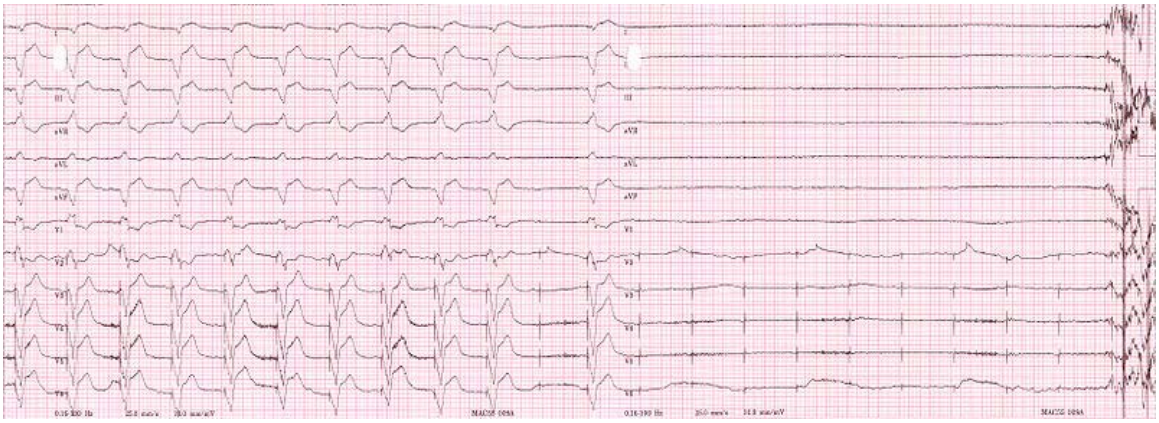
Percussive pacing, also known as transthoracic mechanical pacing, is the use of the closed fist, usually on the left lower edge of the sternum over the right ventricle in the vena cava, striking from a distance of 20 – 30 cm to induce a ventricular beat (the British Journal of Anesthesia suggests this must be done to raise the ventricular pressure to 10 -

15mmHg to induce electrical activity). This is an old procedure used only as a life saving means until an electrical pacemaker is brought to the patient.

Transcutaneous pacing

Transcutaneous pacing (TCP), also called external pacing, is recommended for the initial stabilization of hemodynamically significant bradycardias of all types. The procedure is performed by placing two pacing pads on the patient's chest, either in the anterior/lateral position or the anterior/posterior position. The rescuer selects the pacing rate, and gradually increases the pacing current (measured in mA) until electrical capture (characterized by a wide QRS complex with a tall, broad T wave on the ECG) is achieved, with a corresponding pulse. Pacing artifact on the ECG and severe muscle twitching may make this determination difficult. External pacing should not be relied upon for an extended period of time. It is an emergency procedure that acts as a bridge until transvenous pacing or other therapies can be applied.

Epicardial pacing (temporary)



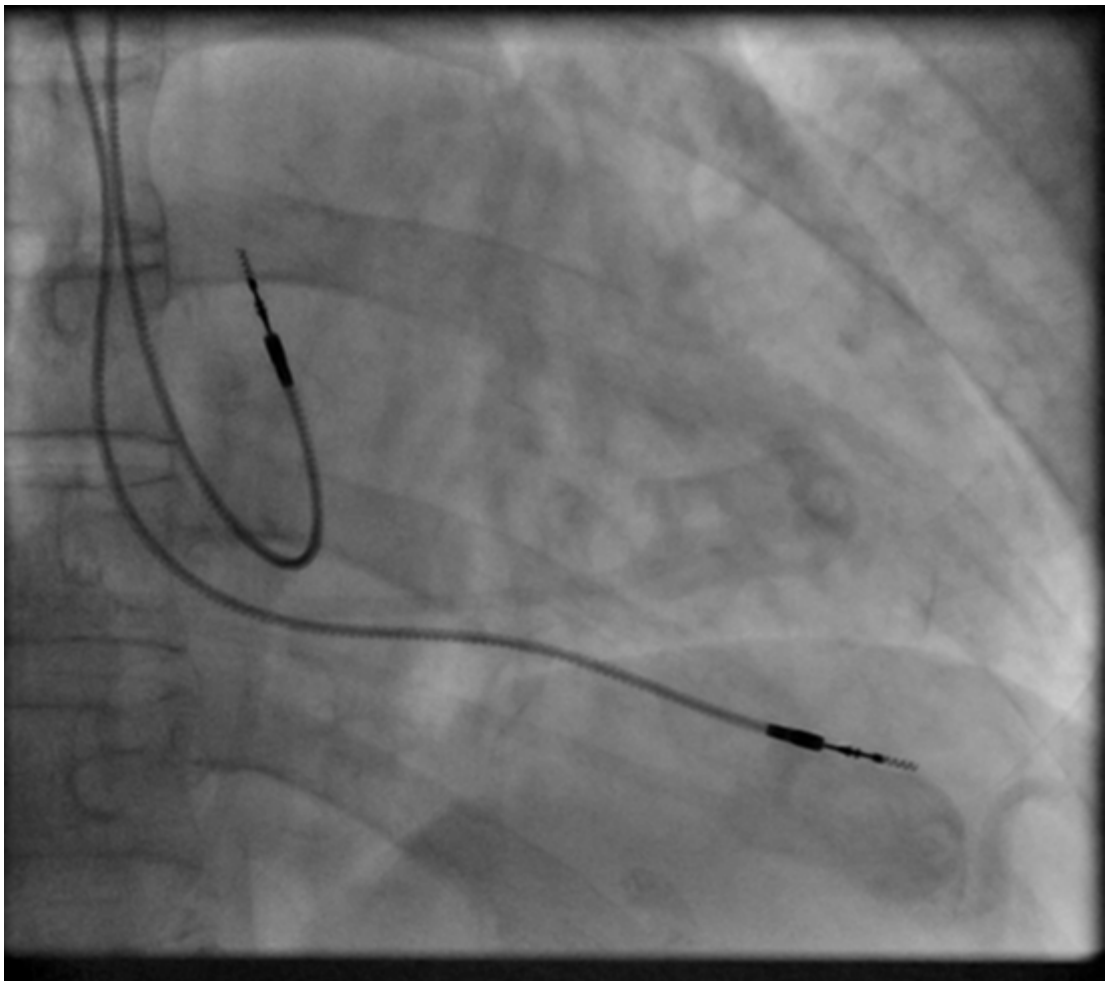
ECG rhythm strip of a threshold determination in a patient with a temporary (epicardial) ventricular pacemaker. The epicardial pacemaker leads were placed after the patient collapsed during aortic valve surgery. In the first half of the tracing, pacemaker stimuli at 60 beats per minute result in a wide QRS complex with a right bundle branch block pattern. Progressively weaker pacing stimuli are administered, which results in asystole in the second half of the tracing. At the end of the tracing, distortion results from muscle contractions due to a (short) hypoxic seizure. Because decreased pacemaker stimuli do not result in a ventricular escape rhythm, the patient can be said to be pacemaker-dependent and needs a definitive pacemaker.

Temporary epicardial pacing is used during open heart surgery should the surgical procedure create atrio ventricular block. The electrodes are placed in contact with the outer wall of the ventricle (epicardium) to maintain satisfactory cardiac output until a temporary transvenous electrode has been inserted.

Transvenous pacing (temporary)

Transvenous pacing, when used for temporary pacing, is an alternative to transcutaneous pacing. A pacemaker wire is placed into a vein, under sterile conditions, and then passed into either the right atrium or right ventricle. The pacing wire is then connected to an external pacemaker outside the body. Transvenous pacing is often used as a bridge to permanent pacemaker placement. It can be kept in place until a permanent pacemaker is implanted or until there is no longer a need for a pacemaker and then it is removed.

Permanent pacing



Right atrial and right ventricular leads as visualized under x-ray during a pacemaker implant procedure. The atrial lead is the curved one making a U shape in the upper left part of the figure.

Permanent pacing with an implantable pacemaker involves transvenous placement of one or more pacing electrodes within a chamber, or chambers, of the heart. The procedure is performed by incision of a suitable vein into which the electrode lead is inserted and passed along the vein, through the valve of the heart, until positioned in the chamber. The procedure is facilitated by fluoroscopy which enables the physician or cardiologist to

view the passage of the electrode lead. After satisfactory lodgement of the electrode is confirmed the opposite end of the electrode lead is connected to the pacemaker generator.

There are three basic types of permanent pacemakers, classified according to the number of chambers involved and their basic operating mechanism:

- *Single-chamber pacemaker*. In this type, only one pacing lead is placed into a chamber of the heart, either the atrium or the ventricle.
- *Dual-chamber pacemaker*. Here, wires are placed in two chambers of the heart. One lead paces the atrium and one paces the ventricle. This type more closely resembles the natural pacing of the heart by assisting the heart in coordinating the function between the atria and ventricles.
- *Rate-responsive pacemaker*. This pacemaker has sensors that detect changes in the patient's physical activity and automatically adjust the pacing rate to fulfill the body's metabolic needs.

The pacemaker generator is a hermetically sealed device containing a power source, usually a lithium battery, a sensing amplifier which processes the electrical manifestation of naturally occurring heart beats as sensed by the heart electrodes, the computer logic for the pacemaker and the output circuitry which delivers the pacing impulse to the electrodes.

Most commonly, the generator is placed below the subcutaneous fat of the chest wall, above the muscles and bones of the chest. However, the placement may vary on a case by case basis.

The outer casing of pacemakers is so designed that it will rarely be rejected by the body's immune system. It is usually made of titanium, which is inert in the body. The whole thing will not be rejected, and will be encapsulated by scar tissue, in the same way a piercing is.

Basic function

Modern pacemakers usually have multiple functions. The most basic form monitors the heart's native electrical rhythm. When the pacemaker fails to sense a heartbeat within a normal beat-to-beat time period, it will stimulate the ventricle of the heart with a short low voltage pulse. This sensing and stimulating activity continues on a beat by beat basis.

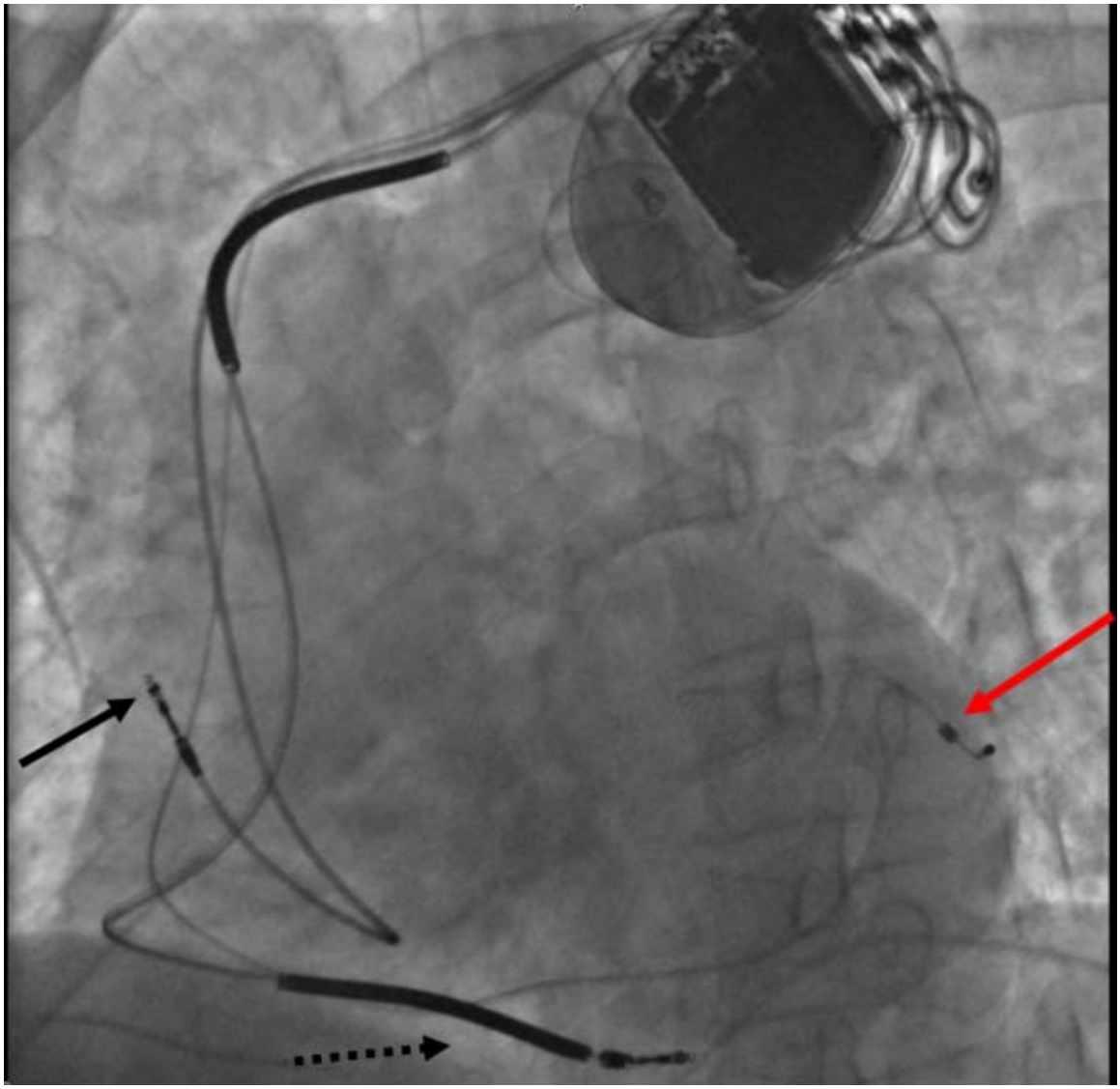
The more complex forms include the ability to sense and/or stimulate both the atrial and ventricular chambers.

The revised NASPE/BPEG generic code for antibradycardia pacing

I	II	III	IV	V
Chamber(s) paced	Chamber(s) sensed	Response to sensing	Rate modulation	Multisite pacing
O = None	O = None	O = None	O = None	O = None
A = Atrium	A = Atrium	T = Triggered	R = Rate modulation	A = Atrium
V = Ventricle	V = Ventricle	I = Inhibited		V = Ventricle
D = Dual (A+V)	D = Dual (A+V)	D = Dual (T+I)		D = Dual (A+V)

From this the basic ventricular "on demand" pacing mode is VVI or with automatic rate adjustment for exercise VVIR - this mode is suitable when no synchronization with the atrial beat is required, as in atrial fibrillation. The equivalent atrial pacing mode is AAI or AAIR which is the mode of choice when atrioventricular conduction is intact but the natural pacemaker the sinoatrial node is unreliable - sinus node disease (SND) or sick sinus syndrome. Where the problem is atrioventricular block (AVB) the pacemaker is required to detect (sense) the atrial beat and after a normal delay (0.1-0.2 seconds) trigger a ventricular beat, unless it has already happened - this is VDD mode and can be achieved with a single pacing lead with electrodes in the right atrium (to sense) and ventricle (to sense and pace). These modes AAIR and VDD are unusual in the US but widely used in Latin America and Europe. The DDDR mode is most commonly used as it covers all the options though the pacemakers require separate atrial and ventricular leads and are more complex, requiring careful programming of their functions for optimal results.

Biventricular pacing (BVP)

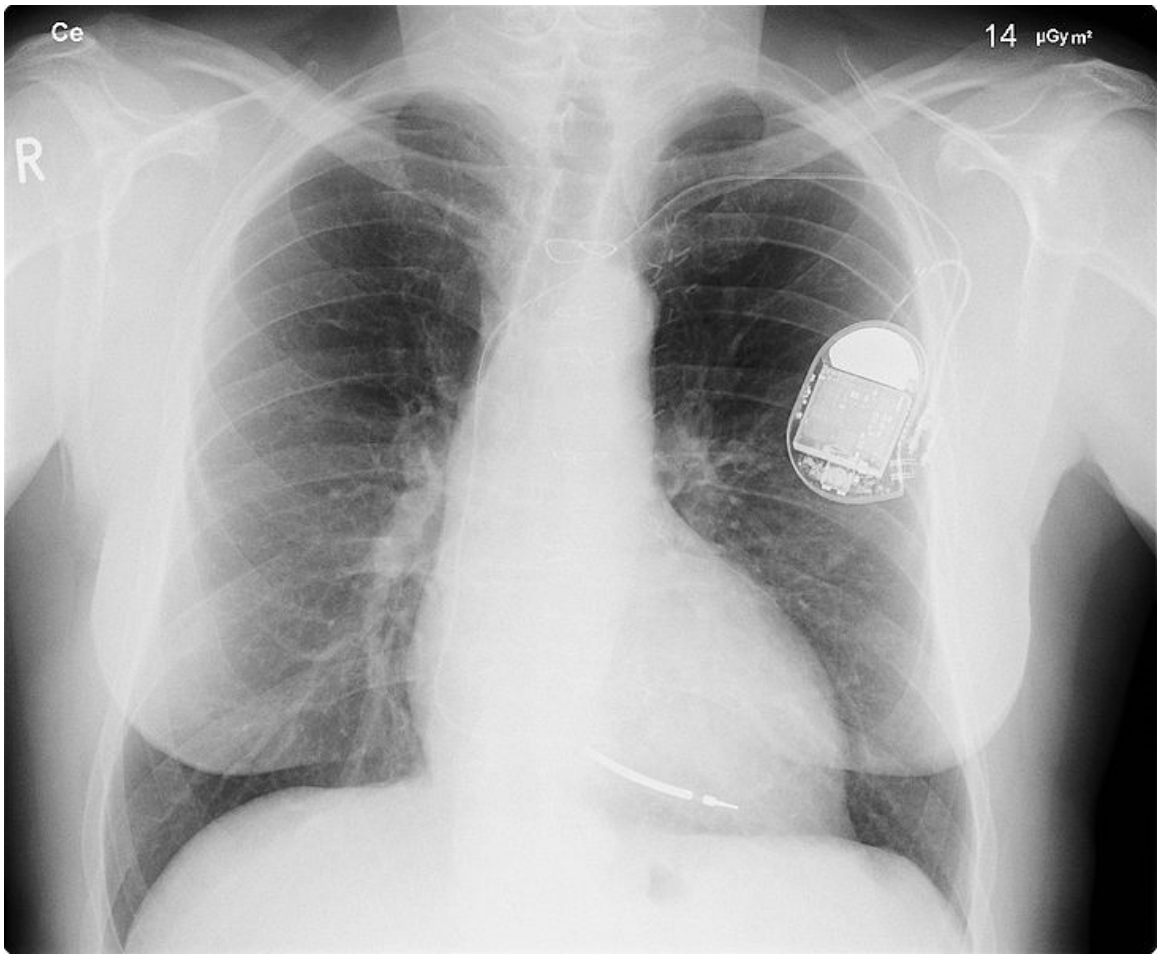


Three leads can be seen in this example of a cardiac resynchronization device: a right atrial lead (solid black arrow), a right ventricular lead (dashed black arrow), and a coronary sinus lead (red arrow). The coronary sinus lead wraps around the outside of the left ventricle, enabling pacing of the left ventricle. Note that the right ventricular lead in this case has 2 thickened aspects that represent conduction coils and that the generator is larger than typical pacemaker generators, demonstrating that this device is both a pacemaker and a cardioverter-defibrillator, capable of delivering electrical shocks for dangerously fast abnormal ventricular rhythms.

A biventricular pacemaker, also known as CRT (cardiac resynchronization therapy) is a type of pacemaker that can pace both the septal and lateral walls of the left ventricle. By pacing both sides of the left ventricle, the pacemaker can resynchronize a heart whose opposing walls do not contract in synchrony, which occurs in approximately 25-50 % of heart failure patients. CRT devices have at least two leads, one in the right ventricle to

stimulate the septum, and another inserted through the coronary sinus to pace the lateral wall of the left ventricle. Often, for patients in normal sinus rhythm, there is also a lead in the right atrium to facilitate synchrony with the atrial contraction. Thus, timing between the atrial and ventricular contractions, as well as between the septal and lateral walls of the left ventricle can be adjusted to achieve optimal cardiac function. CRT devices have been shown to reduce mortality and improve quality of life in patients with heart failure symptoms; a LV ejection fraction less than or equal to 35% and QRS duration on EKG of 120 msec or greater. CRT can be combined with an implantable cardioverter-defibrillator (ICD).

Advancements in function



X-ray image of installed pacemaker showing wire routing

A major step forward in pacemaker function has been to attempt to mimic nature by utilizing various inputs to produce a rate-responsive pacemaker using parameters such as the QT interval, pO_2 - pCO_2 (dissolved oxygen or carbon dioxide levels) in the arterial-venous system, physical activity as determined by an accelerometer, body temperature, ATP levels, adrenaline, etc. Instead of producing a static, predetermined heart rate, or intermittent control, such a pacemaker, a 'Dynamic Pacemaker', could compensate for

both actual respiratory loading and potentially anticipated respiratory loading. The first dynamic pacemaker was invented by Dr. Anthony Rickards of the National Health Hospital, London, UK, in 1982.

Dynamic pacemaking technology could also be applied to future artificial hearts. Advances in transitional tissue welding would support this and other artificial organ/joint/tissue replacement efforts. Stem cells may or may not be of interest to transitional tissue welding.

Many advancements have been made to improve the control of the pacemaker once implanted. Many of these have been made possible by the transition to microprocessor controlled pacemakers. Pacemakers that control not only the ventricles but the atria as well have become common. Pacemakers that control both the atria and ventricles are called dual-chamber pacemakers. Although these dual-chamber models are usually more expensive, timing the contractions of the atria to precede that of the ventricles improves the pumping efficiency of the heart and can be useful in congestive heart failure.

Rate responsive pacing allows the device to sense the physical activity of the patient and respond appropriately by increasing or decreasing the base pacing rate via rate response algorithms.

The DAVID trials have shown that unnecessary pacing of the right ventricle can lead to heart failure and an increased incidence of atrial fibrillation. The newer dual chamber devices can keep the amount of right ventricle pacing to a minimum and thus prevent worsening of the heart disease.

Considerations

Insertion

A pacemaker is typically inserted into the patient through a simple surgery using either local anesthetic or a general anesthetic. The patient may be given a drug for relaxation before the surgery as well. An antibiotic is typically administered to prevent infection. In most cases the pacemaker is inserted in the left shoulder area where an incision is made below the collar bone creating a small pocket where the pacemaker is actually housed in the patient's body. The lead or leads (the number of leads varies depending on the type of pacemaker) are fed into the heart through a large vein using a fluoroscope to monitor the progress of lead insertion. The Right Ventricular lead would be positioned away from the apex (tip) of the right ventricle and up on the inter ventricular septum, below the outflow tract, to prevent deterioration of the strength of the heart. The actual surgery may take about 30 to 90 minutes.

Following surgery the patient should exercise reasonable care about the wound as it heals. There is a followup session during which the pacemaker is checked using a "programmer" that can communicate with the device and allows a health care professional to evaluate the system's integrity and determine the settings such as pacing

voltage output. The patient should have the strength of their heart analyzed frequently with echocardiography, every 1 or 2 years, to make sure the that placement of the right ventricular lead has not lead to weakening of the left ventricle.

The patient may want to consider some basic preparation before the surgery. The most basic preparation is that people who have body hair on the chest may want to remove the hair by shaving or using a depilatory agent as the surgery will involve bandages and monitoring equipment to be afixed to the body.

Since a pacemaker uses batteries, the device itself will need replacement as the batteries lose power. Device replacement is usually a simpler procedure than the original insertion as it does not normally require leads to be implanted. The typical replacement requires a surgery in which an incision is made to remove the existing device, the leads are removed from the existing device, the leads are attached to the new device, and the new device is inserted into the patient's body replacing the previous device.

Pacemaker patient identification card

International pacemaker patient identification cards carry information such as; patient data (between others, symptom primary, ECG, aetiology), pacemaker center (doctor, hospital), IPG (rate, mode, date of implantation, MFG, type) and lead.

Living with a pacemaker

Periodic pacemaker checkups

Two types of remote monitoring devices used by pacemaker patients.

Once the pacemaker is implanted, it is periodically checked to ensure the device is operational and performing appropriately. Depending on the frequency set by the

following physician, the device can be checked as often as is necessary. Routine pacemaker checks are typically done in-office every six (6) months, though will vary depending upon patient/device status and remote monitoring availability.

At the time of in-office follow-up, the device will be interrogated to perform diagnostic testing. These tests include:

- Sensing: the ability of the device to "see" intrinsic cardiac activity (Atrial and ventricular depolarization).
- Impedance: A test to measure lead integrity. Large and/or sudden increases in impedance can be indicative of a lead fracture while large and/or sudden decreases in impedance can signify a breach in lead insulation.
- Threshold: this test confirms the minimum amount of energy (Both volts and pulse width) required to reliably depolarize (capture) the chamber being tested. Determining the threshold allows the Allied Professional, Representative, or Physician to program an output that recognizes an appropriate safety margin while optimizing device longevity.

As modern pacemakers are "on-demand", meaning that they only pace when necessary, device longevity is affected by how much it is utilized. Other factors affecting device longevity include programmed output and algorithms (features) causing a higher level of current drain from the battery.

An additional aspect of the in-office check is to examine any events that were stored since the last follow-up. These are typically stored based on specific criteria set by the physician and specific to the patient. Some devices have the availability to display intracardiac electrograms of the onset of the event as well as the event itself. This is especially helpful in diagnosing the cause or origin of the event and making any necessary programming changes.

Lifestyle considerations

A patient's lifestyle is usually not modified to any great degree after insertion of a pacemaker. There are a few activities that are unwise such as full contact sports and activities that involve intense magnetic fields.

The pacemaker patient may find that some types of everyday actions need to be modified. For instance, the shoulder harness of a vehicle seatbelt may be uncomfortable if the harness should fall across the pacemaker insertion site.

Any kind of an activity that involves intense magnetic fields should be avoided. This includes activities such as arc welding possibly, with certain types of equipment, or maintaining heavy equipment that may generate intense magnetic fields (such as an MRI (Magnetic Resonance Imaging Machine)).

However, in February 2011 the FDA approved a new pacemaker device called the Revo MRI SureScan which is the first to be proven safe for MRI use. There are several limitations to its use including certain patients qualifications, body parts, and scan settings.

A 2008 U.S. study has found that the magnets in some portable music players, when placed within an inch of pacemakers, may cause interference.

Some medical procedures may require the use of antibiotics to be administered before the procedure. The patient should inform all medical personnel that they have a pacemaker. Some standard medical procedures such as the use of Magnetic resonance imaging (MRI) may be ruled out by the patient having a pacemaker.

In addition, according to the American Heart Association, some home devices have a remote potential to cause interference by occasionally inhibiting a single beat. Cellphones available in the United States (less than 3 watts) do not seem to damage pulse generators or affect how the pacemaker works.

Turning off the pacemaker

According to a consensus statement by the Heart Rhythm Society, it is legal and ethical to honor requests by patients, or by those with legal authority to make decisions for patients, to deactivate implanted cardiac devices. Lawyers say that the legal situation is similar to removing a feeding tube. A patient has a right to refuse or discontinue treatment, including a pacemaker that keeps him or her alive. Physicians have a right to refuse to turn it off, but they should refer the patient to a physician who will. Some patients believe that hopeless, debilitating conditions like strokes, in combination with dementia, can cause so much suffering to themselves and their families that they would prefer not to prolong their lives with supportive measures, such as cardiac devices.

Privacy and security

Security and privacy concerns have been raised with pacemakers that allow wireless communication. Unauthorized third parties may be able to read patient records contained in the pacemaker, or reprogram the devices, as has been demonstrated by a team of researchers. The demonstration worked at short range; they did not attempt to develop a long range antenna. The proof of concept exploit helps demonstrate the need for better security and patient alerting measures in remotely accessible medical implants.

Complications

A possible complication of dual-chamber artificial pacemakers is *pacemaker-mediated tachycardia* (PMT), a form of reentrant tachycardia. In PMT, the artificial pacemaker forms the anterograde (atrium to ventricle) limb of the circuit and the atrioventricular (AV) node forms the retrograde limb (ventricle to atrium) of the circuit. Treatment of PMT typically involves reprogramming the pacemaker.

Other devices with pacemaker function

Sometimes devices resembling pacemakers, called implantable cardioverter-defibrillators (ICDs) are implanted. These devices are often used in the treatment of patients at risk from sudden cardiac death. An ICD has the ability to treat many types of heart rhythm disturbances by means of pacing, cardioversion, or defibrillation. Some ICD devices can distinguish between ventricular fibrillation and ventricular tachycardia (VT), and may try to pace the heart faster than its intrinsic rate in the case of VT, to try to break the tachycardia before it progresses to ventricular fibrillation. This is known as *fast-pacing*, *overdrive pacing*, or *anti-tachycardia pacing* (ATP). ATP is only effective if the underlying rhythm is ventricular tachycardia, and is never effective if the rhythm is ventricular fibrillation.

NASPE / BPEG Defibrillator (NBD) code - 1993

I	**II**	**III**	**IV**
Shock chamber	Antitachycardia pacing chamber	Tachycardia detection	Antibradycardia pacing chamber
O = None	O = None	E = Electrogram	O = None
A = Atrium	A = Atrium	H = Hemodynamic	A = Atrium
V = Ventricle	V = Ventricle		V = Ventricle
D = Dual (A+V)	D = Dual (A+V)		D = Dual (A+V)

Short form of the NASPE/BPEG Defibrillator (NBD) code

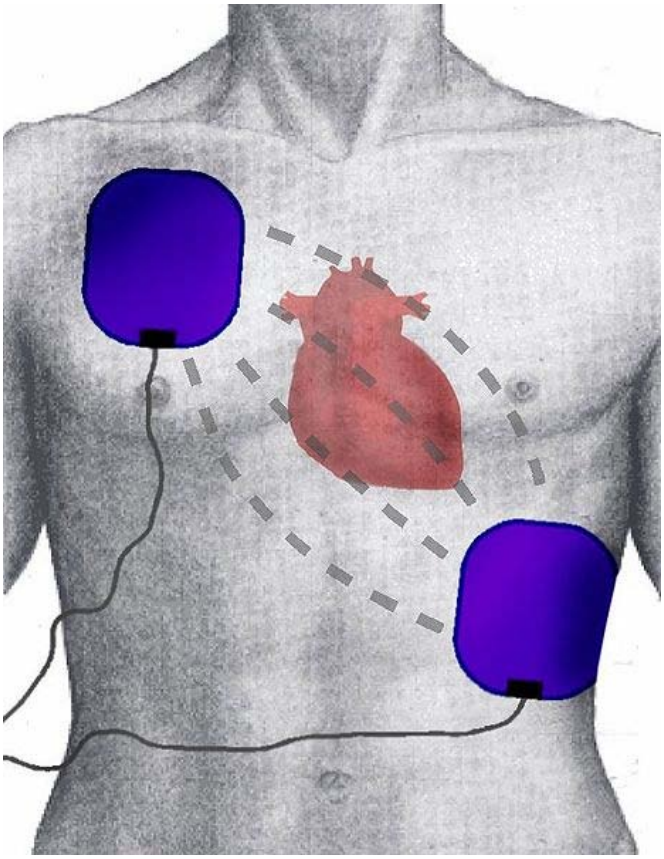
ICD-S ICD with shock capability only

ICD-B ICD with bradycardia pacing as well as shock

ICD-T ICD with tachycardia (and bradycardia) pacing as well as shock

Chapter 8

Defibrillation



View of defibrillator position and placement, using hands free electrodes.

Defibrillation is the definitive treatment for the life-threatening cardiac arrhythmias, ventricular fibrillation and pulseless ventricular tachycardia. Defibrillation consists of delivering a therapeutic dose of electrical energy to the affected heart with a device called a **defibrillator**. This depolarizes a critical mass of the heart muscle, terminates the arrhythmia, and allows normal sinus rhythm to be reestablished by the body's natural pacemaker, in the sinoatrial node of the heart. Defibrillators can be external, transvenous,

or implanted, depending on the type of device used or needed. Some external units, known as automated external defibrillators (AEDs), automate the diagnosis of treatable rhythms, meaning that lay responders or bystanders are able to use them successfully with little, or in some cases no training at all.

History

Defibrillation was first demonstrated in 1899 by Jean Louis Prevost and Frederic Batelli, two physiologists from University of Geneva, Switzerland. They discovered that small electric shocks could induce ventricular fibrillation in dogs, and that larger charges would reverse the condition.

In 1933 a Dr Albert Hyman a heart specialist at the Beth Davis Hospital of New York city and a C. Henry Hyman, an electrical engineer, looking for an alternative to injecting powerful drugs directly into the heart, came up with an invention that used an electrical shock in place of drug injection. This invention was called the *Hyman Otor* where a hollow needle is used to pass an insulated wire to the heart area to deliver the electrical shock. The hollow steel needle being one end of the circuit and the insulated wire the other end. Whether the *Hyman Otor* was a success is unknown.

The first use on a human was in 1947 by Claude Beck, professor of surgery at Case Western Reserve University. Beck's theory was that ventricular fibrillation often occurred in hearts which were fundamentally healthy, in his terms "Hearts that are too good to die", and that there must be a way of saving them. Beck first used the technique successfully on a 14 year old boy who was being operated on for a congenital chest defect. The boy's chest was surgically opened, and manual cardiac massage was undertaken for 45 minutes until the arrival of the defibrillator. Beck used internal paddles on either side of the heart, along with procainamide, an antiarrhythmic drug, and achieved return of normal sinus rhythm.

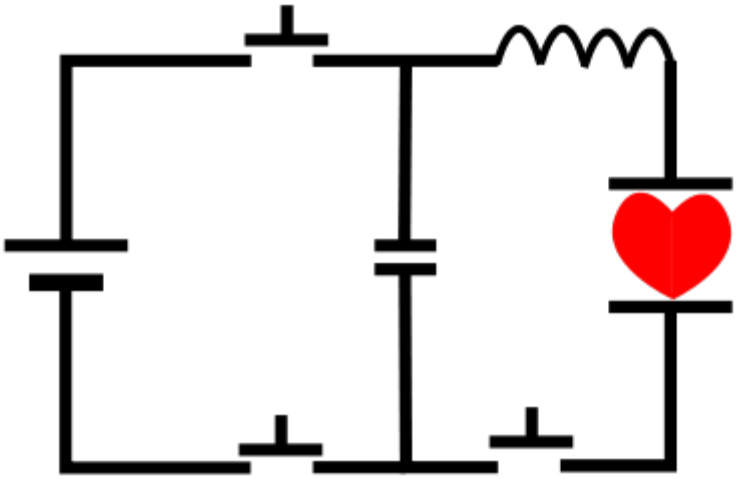
These early defibrillators used the alternating current from a power socket, transformed from the 110-240 volts available in the line, up to between 300 and 1000 volts, to the exposed heart by way of 'paddle' type electrodes. The technique was often ineffective in reverting VF while morphological studies showed damage to the cells of the heart muscle post mortem. The nature of the AC machine with a large transformer also made these units very hard to transport, and they tended to be large units on wheels.

Closed-chest method

Until the early 1950s, defibrillation of the heart was possible only when the chest cavity was open during surgery. The technique used an alternating current from a 300 or greater volt source delivered to the sides of the exposed heart by 'paddle' electrodes where each electrode was a flat or slightly concave metal plate of about 40 mm diameter. The closed-chest defibrillator device which applied an alternating current of greater than 1000 amps, conducted by means of externally applied electrodes through the chest cage to the heart,

was pioneered by Dr V. Eskin with assistance by A. Klimov in Frunze, USSR (today known as Bishkek, Kyrgyzstan) in mid 1950s.

Move to direct current



A circuit diagram showing the simplest (non-electronically controlled) defibrillator design, depending on the inductor (damping), producing a Lown, Edmark or Gurvich Waveform

In 1959 Bernard Lown commenced research into an alternative technique which involved charging of a bank of capacitors to approximately 1000 volts with an energy content of 100-200 joules then delivering the charge through an inductance such as to produce a heavily damped sinusoidal wave of finite duration (~5 milliseconds) to the heart by way of 'paddle' electrodes. The work of Lown was taken to clinical application by engineer Barouh Berkovits with his "cardioverter".

The Lown waveform, as it was known, was the standard for defibrillation until the late 1980s when numerous studies showed that a biphasic truncated waveform (BTE) was equally efficacious while requiring the delivery of lower levels of energy to produce defibrillation. A side effect was a significant reduction in weight of the machine. The BTE waveform, combined with automatic measurement of transthoracic impedance is the basis for modern defibrillators.

Portable units become available

A major breakthrough was the introduction of portable defibrillators used out of the hospital. This was pioneered in the early 1960s by Prof. Frank Pantridge in Belfast. Today portable defibrillators are among the many very important tools carried by ambulances. They are the only proven way to resuscitate a person who has had a cardiac arrest unwitnessed by EMS who is still in persistent ventricular fibrillation or ventricular tachycardia at the arrival of pre-hospital providers.

Gradual improvements in the design of defibrillators, partly based on the work developing implanted versions, have led to the availability of Automated External Defibrillators. These devices can analyse the heart rhythm by themselves, diagnose the shockable rhythms, and charge to treat. This means that no clinical skill is required in their use, allowing lay people to respond to emergencies effectively.

Change to a biphasic waveform

Until the late 1980s, external defibrillators delivered a Lown type waveform which was a heavily damped sinusoidal impulse having a mainly uniphasic characteristic. Biphasic defibrillation, alternates the direction of the pulses, completing one cycle in approximately 10 milliseconds. Biphasic defibrillation was originally developed and used for implantable cardioverter-defibrillators. When applied to external defibrillators, biphasic defibrillation significantly decreases the energy level necessary for successful defibrillation, decreasing the risk of burns and myocardial damage.

Ventricular fibrillation (VF) could be returned to normal sinus rhythm in 60% of cardiac arrest patients treated with a single shock from a monophasic defibrillator. Most biphasic defibrillators have a first shock success rate of greater than 90%.

Implantable devices

A further development in defibrillation came with the invention of the implantable device, known as an implantable cardioverter-defibrillator (or ICD). This was pioneered at Sinai Hospital in Baltimore by a team that included Stephen Heilman, Alois Langer, Jack Lattuca, Morton Mower, Michel Mirowski, and Mir Imran, with the help of industrial collaborator Intec Systems of Pittsburgh. Mirowski teamed up with Mower and Staewen, and together they commenced their research in 1969 but it was 11 years before they treated their first patient. Similar developmental work was carried out by Schuder and colleagues at the University of Missouri.

The work was commenced, despite doubts amongst leading experts in the field of arrhythmias and sudden death. There was doubt that their ideas would ever become a clinical reality. In 1962 Bernard Lown introduced the external DC defibrillator. This device applied a direct current from a discharging capacitor through the chest wall into the heart to stop heart fibrillation. In 1972, Lown stated in the journal *Circulation* - "The very rare patient who has frequent bouts of ventricular fibrillation is best treated in a coronary care unit and is better served by an effective antiarrhythmic program or surgical correction of inadequate coronary blood flow or ventricular malfunction. In fact, the implanted defibrillator system represents an imperfect solution in search of a plausible and practical application."

The problems to be overcome were the design of a system which would allow detection of ventricular fibrillation or ventricular tachycardia. Despite the lack of financial backing and grants, they persisted and the first device was implanted in February 1980 at Johns

Hopkins Hospital by Dr. Levi Watkins, Jr. Modern ICDs do not require a thoracotomy and possess pacing, cardioversion, and defibrillation capabilities.

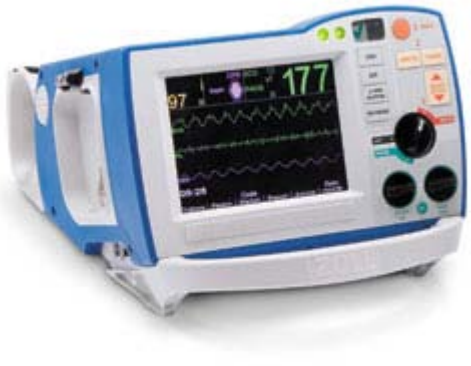
The invention of implantable units is invaluable to some regular sufferers of heart problems, although they are generally only given to those people who have already had a cardiac episode.

Types

Manual external defibrillator

External defibrillator / monitor

The units are used in conjunction with (or more often have inbuilt) electrocardiogram readers, which the healthcare provider uses to diagnose a cardiac condition (most often fibrillation or tachycardia although there are some other rhythms which can be treated by different shocks).



Manual external defibrillator monitor

The healthcare provider will then decide what charge (in joules) to use, based on proven guidelines and experience, and will deliver the shock through paddles or pads on the patient's chest. As they require detailed medical knowledge, these units are generally only found in hospitals and on some ambulances. For instance, every NHS ambulance in the United Kingdom is equipped with a manual defibrillator for use by the attending paramedics and technicians. In the United States, many advanced EMTs and all paramedics are trained to recognize lethal arrhythmias and deliver appropriate electrical therapy with a manual defibrillator when appropriate.

Manual internal defibrillator

These are the direct descendants of the work of Beck and Lown. They are virtually identical to the external version, except that the charge is delivered through internal paddles in direct contact with the heart. These are almost exclusively found in operating theatres, where the chest is likely to be open, or can be opened quickly by a surgeon.

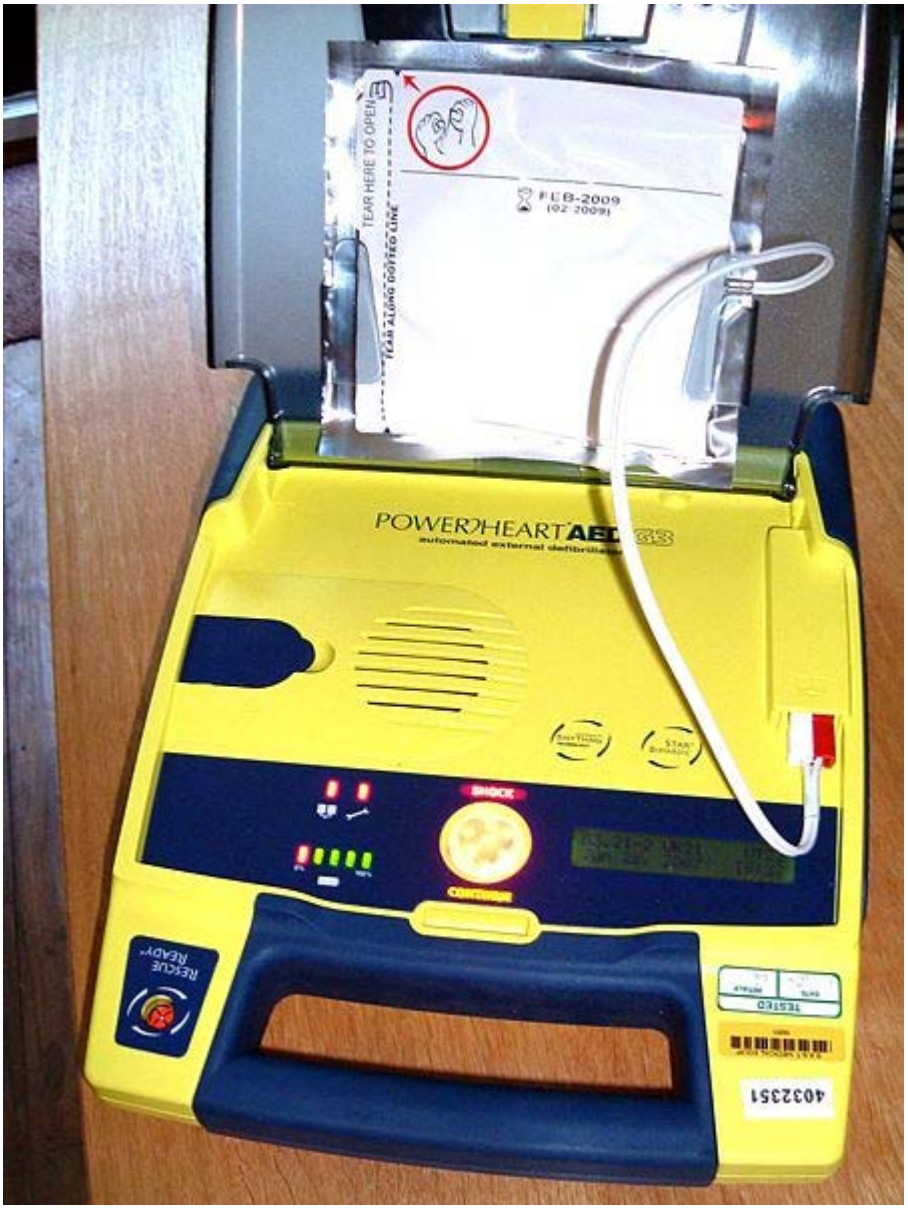
Automated external defibrillator (AED)

An AED at a railway station in Japan. The AED box has information on how to use it in Japanese, English, Chinese and Korean, and station staff are trained to use it.

These simple-to-use units are based on computer technology which is designed to analyze the heart rhythm itself, and then advise the user whether a shock is required. They are designed to be used by lay persons, who require little training to operate them correctly. They are usually limited in their interventions to delivering high joule shocks for VF (ventricular fibrillation) and VT (ventricular tachycardia) rhythms, making them generally of limited use to health professionals, who could diagnose and treat a wider range of problems with a manual or semi-automatic unit.

The automatic units also take time (generally 10–20 seconds) to diagnose the rhythm, where a professional could diagnose and treat the condition far more quickly with a manual unit. These time intervals for analysis, which require stopping chest compressions, have been shown in a number of studies to have a significant negative effect on shock success. This effect led to the recent change in the AHA defibrillation guideline (calling for two minutes of CPR after each shock without analyzing the cardiac rhythm) and some bodies recommend that AEDs should not be used when manual defibrillators and trained operators are available.

Automated external defibrillators are generally either held by trained personnel who will attend incidents, or are **public access** units which can be found in places including corporate and government offices, shopping centres, airports, restaurants, casinos, hotels, sports stadiums, schools and universities, community centers, fitness centers and health clubs.



An automated external defibrillator, open and ready for pads to be attached

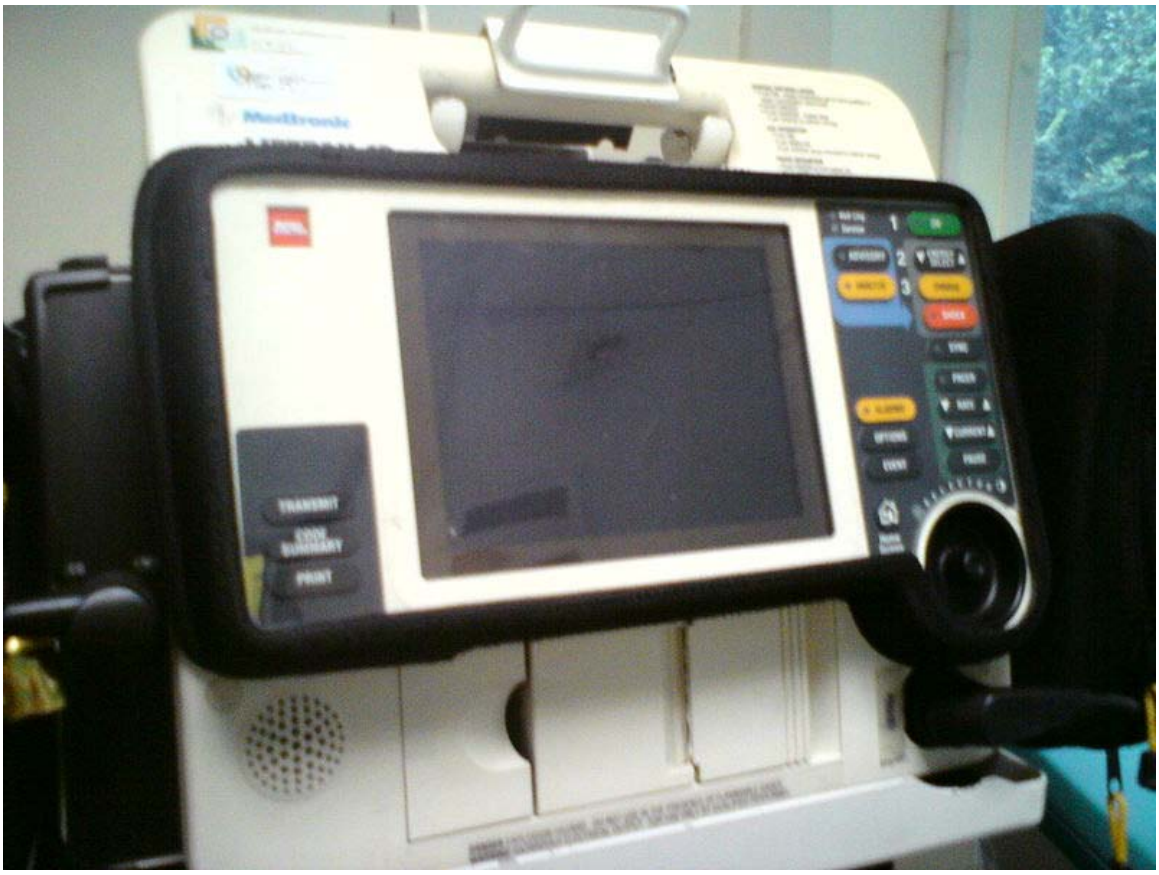
The locating of a public access AED should take in to account where large groups of people gather, and the risk category associated with these people, to ascertain whether the risk of a sudden cardiac arrest incident is high. For example, a center for teenage children is a particularly low risk category (as children very rarely enter heart rhythms such as VF (Ventricular Fibrillation) or VT (Ventricular Tachycardia), being generally young and fit, and the most common causes of pediatric cardiac arrest are respiratory arrest and trauma - where the heart is more likely to enter asystole or PEA, (where an AED is of no use). On the other hand, a large office building with a high ratio of males over 50 is a very high risk environment.

Automated-external-defibrillator

In many areas, emergency services vehicles are likely to carry AEDs. EMT-Basics in most areas are not trained in manual defibrillation, and often carry an AED instead. Some ambulances carry an AED in addition to a manual unit. In addition, some police or fire service vehicles carry an AED for first responder use. Some areas have dedicated community first responders, who are volunteers tasked with keeping an AED and taking it to any victims in their area. It is also increasingly common to find AEDs on transport such as commercial airlines and cruise ships. The presence of an AED can be a particularly decisive factor in cardiac patient survival in these scenarios, as professional medical assistance may be hours away.

In order to make them highly visible, public access AEDs often are brightly coloured, and are mounted in protective cases near the entrance of a building. When these protective cases are opened, and the defibrillator removed, some will sound a buzzer to alert nearby staff to their removal but do not necessarily summon emergency services. All trained AED operators should also know to phone for an ambulance when sending for or using an AED, as the patient will be unconscious, which always requires ambulance attendance.

Semi-automated external defibrillators



A Lifepak semi-automatic defibrillator/ECG monitor mounted in an ambulance. These units are designed for use only by healthcare professionals and are capable of measuring blood pressure and blood oxygen saturation in addition to the primary functions.

These units are a compromise between a full manual unit and an automated unit. They are mostly used by pre-hospital care professionals such as paramedics and emergency medical technicians. These units have the automated capabilities of the AED but also feature an ECG display, and a manual override, where the clinician can make their own decision, either before or instead of the computer. Some of these units are also able to act as a pacemaker if the heart rate is too slow (bradycardia) and perform other functions which require a skilled operator.

Implantable cardioverter-defibrillator (ICD)

Also known as automatic internal cardiac defibrillator (AICD). These devices are implants, similar to pacemakers (and many can also perform the pacemaking function). They constantly monitor the patient's heart rhythm, and automatically administer shocks for various life threatening arrhythmias, according to the device's programming. Many modern devices can distinguish between ventricular fibrillation, ventricular tachycardia, and more benign arrhythmias like supraventricular tachycardia and atrial fibrillation. Some devices may attempt overdrive pacing prior to synchronised cardioversion. When

the life threatening arrhythmia is ventricular fibrillation, the device is programmed to proceed immediately to an unsynchronized shock.

There are cases where the patient's ICD may fire constantly or inappropriately. This is considered a medical emergency, as it depletes the device's battery life, causes significant discomfort and anxiety to the patient, and in some cases may actually trigger life threatening arrhythmias. Some emergency medical services personnel are now equipped with a ring magnet to place over the device, which effectively disables the shock function of the device while still allowing the pacemaker to function (if the device is so equipped). If the device is shocking frequently, but appropriately, EMS personnel may administer sedation.

Wearable cardiac defibrillator

A development of the AICD is a portable external defibrillator that is worn like a vest. The unit monitors the patient 24 hours a day and will automatically deliver a biphasic shock if needed. This device is mainly indicated in patients awaiting an implantable defibrillator. Currently only one company manufactures these and they are of limited availability.

Modelling defibrillation

The efficacy of a cardiac defibrillator is highly dependent on the position of its electrodes. Most internal defibrillators are implanted in octogenarians, but a few children need the devices. Implanting defibrillators in kids is particularly difficult because children are small, will grow over time, and possess cardiac anatomy that differs from that of adults. Recently, researchers were able to create a software modeling system capable of mapping an individual’s thorax and determining the optimal position for an external or internal cardiac defibrillator.

With the help of pre-existing surgical planning applications, the software uses myocardial voltage gradients to predict the likelihood of successful defibrillation. According to the critical mass hypothesis, defibrillation is effective only if it produces a threshold voltage gradient in a large fraction of the myocardial mass. Usually, a gradient of three to five volts per centimeter is needed in 95 % of the heart. Voltage gradients of over 60 V/cm can damage tissue. The modeling software seeks to obtain safe voltage gradients above the defibrillation threshold.

Early simulations using the software suggest that small changes in electrode positioning can have large effects on defibrillation, and despite engineering hurdles that remain, the modeling system promises to help guide the placement of implanted defibrillators in children and adults.

Recent mathematical models of defibrillation are based on the bidomain model of cardiac tissue. Calculations using a realistic heart shape and fiber geometry are required to determine how cardiac tissue responds to a strong electrical shock.

Interface with the patient

The most well-known type of electrode (widely depicted in films and television) is the traditional metal paddle with an insulated (usually plastic) handle. This type must be held in place on the patient's skin while a shock or a series of shocks is delivered. Before the paddle is used, a gel must be applied to the patient's skin, in order to ensure a good connection and to minimize electrical resistance, also called chest impedance (despite the DC discharge). These are generally only found on the manual external units.

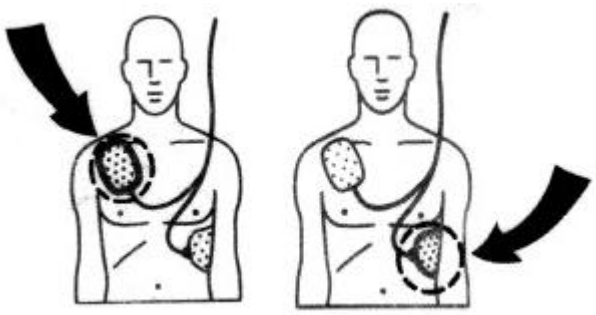
Newer types of resuscitation electrodes are designed as an adhesive pad. These are peeled off their backing and applied to the patient's chest when deemed necessary, much the same as any other sticker. These electrodes are then connected to a defibrillator. If defibrillation is required, the machine is charged, and the shock is delivered, without any need to apply any gel or to retrieve and place any paddles. These adhesive pads are found on most automated and semi-automated units, and are gradually replacing paddles entirely in non-hospital settings.

Both solid- and wet-gel adhesive electrodes are available. Solid-gel electrodes are more convenient, because there is no need to clean the patient's skin after removing the electrodes. However, the use of solid-gel electrodes presents a higher risk of burns during defibrillation, since wet-gel electrodes more evenly conduct electricity into the body.

Some adhesive electrodes are designed to be used not only for defibrillation, but also for transcutaneous pacing and synchronized electrical cardioversion.

In a hospital setting, paddles are generally preferred to pads, due to the inherent speed with which they can be placed and used. This is critical during cardiac arrest, as each second of nonperfusion means tissue loss. However, in cases in which cardiac arrest is suspected, patches placed prophalactically are superior,as they provide appropriate EKG tracing without the artifact visible from human interference with the paddles. Adhesive electrodes are also inherently safer than the paddles for the operator of the defibrillator to use, as they minimize the risk of the operator coming into physical (and thus electrical) contact with the patient as the shock is delivered, by allowing the operator to stand several feet away. Adhesive patches also require no force to remain in place and deliver the shock appropriately, whereas paddles require approximately 25 lbs of force to be applied while the shock is delivered.

Placement



Anterio-apical placement of external defibrillator electrodes (When defibrillation is unsuccessful, anterior-posterior placement is also sometimes attempted)

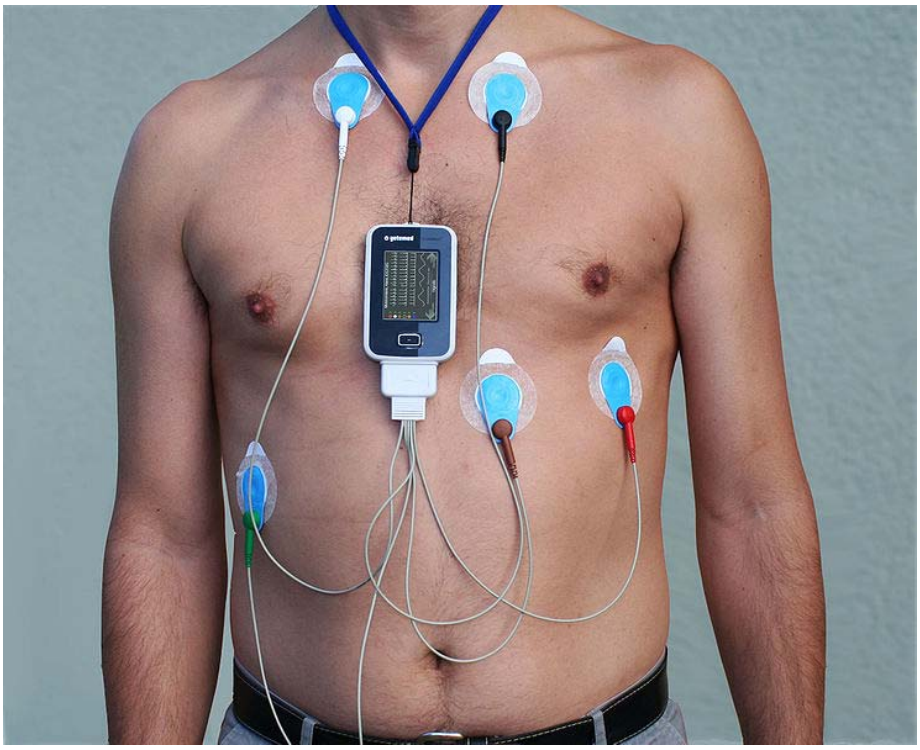
Resuscitation electrodes are placed according to one of two schemes. The anterior-posterior scheme (conf. image) is the preferred scheme for long-term electrode placement. One electrode is placed over the left precordium (the lower part of the chest, in front of the heart). The other electrode is placed on the back, behind the heart in the region between the scapula. This placement is preferred because it is best for non-invasive pacing.

The anterior-apex scheme can be used when the anterior-posterior scheme is inconvenient or unnecessary. In this scheme, the anterior electrode is placed on the right, below the clavicle. The apex electrode is applied to the left side of the patient, just below and to the left of the pectoral muscle. This scheme works well for defibrillation and cardioversion, as well as for monitoring an ECG.

Chapter 9

Holter Monitor

Holter monitor



Holter monitor

Inventor Norman Holter

In medicine, a **Holter monitor** (often simply "Holter" or occasionally **ambulatory electrocardiography device**) is a portable device for continuously monitoring various electrical activity of the central nervous system for at least 24 hours (modern Holters allow up to 11 days of monitoring). The Holter's most common use is for monitoring heart activity (electrocardiography or ECG), but it can also be used for monitoring brain

activity (electroencephalography or EEG). Its extended recording period is sometimes useful for observing occasional cardiac arrhythmias or epileptic events which would be difficult to identify in a shorter period of time. For patients having more transient symptoms, a cardiac event monitor which can be worn for a month or more can be used.

The Holter monitor is named for physicist Norman J. Holter who invented telemetric cardiac monitoring in 1949. Clinical use started in the early 1960s.

When used for the heart, much like standard electrocardiography the Holter monitor records electrical signals from the heart via a series of electrodes attached to the chest. Electrodes are placed over bones to minimize artifacts from muscular activity. The number and position of electrodes varies by model, but most Holter monitors employ between three and eight. These electrodes are connected to a small piece of equipment that is attached to the patient's belt or hung around the neck, and is responsible for keeping a log of the heart's electrical activity throughout the recording period.

Older devices used reel to reel tapes or a standard C90 or C120 audio cassette and ran at a 1.7mm or 2mm/second speed to record the data. Once a recording was made, it could be played back and analysed at 60x speed so 24 hours of recording could be analysed in 24 minutes. More modern units record onto digital flash memory devices. The data are uploaded into a computer which then automatically analyzes the input, counting ECG complexes, calculating summary statistics such as average heart rate, minimum and maximum heart rate, and finding candidate areas in the recording worthy of further study by the technician.

Recorder

Each Holter system consists of two basic parts – the hardware (called monitor or recorder) for recording the signal and software for review and analysis of the record. Advanced Holter recorders are able to display the signal, which is very useful for checking the signal quality. Very often there is also a “patient button” located on the front site allowing the patient to press it in specific cases such as sickness, going to bed, taking pills…. A special mark will be then placed into the record so that the doctors or technicians can quickly pinpoint these areas when analyzing the signal. More modern devices also have the ability to record a vocal patient diary entry.

Size of recorder differs depending on manufacturer of the device. The average dimensions of today’s Holter monitors are about 110x70x30 mm. Most of the devices operate with two AA batteries. In case the batteries die, some Holters allow their replacement even during monitoring.

Most of the Holters monitor the ECG just in 2 or 3 channels. Depending on the model (manufacturer), different count of leads and lead systems are used. Today’s trend is to minimize such number to insure the patient’s comfort during recording. Although 2/3 channel recording has been used for a long time in the Holter monitoring history, recently 12 channel Holters have appeared. These systems use the classic Mason-Likar lead

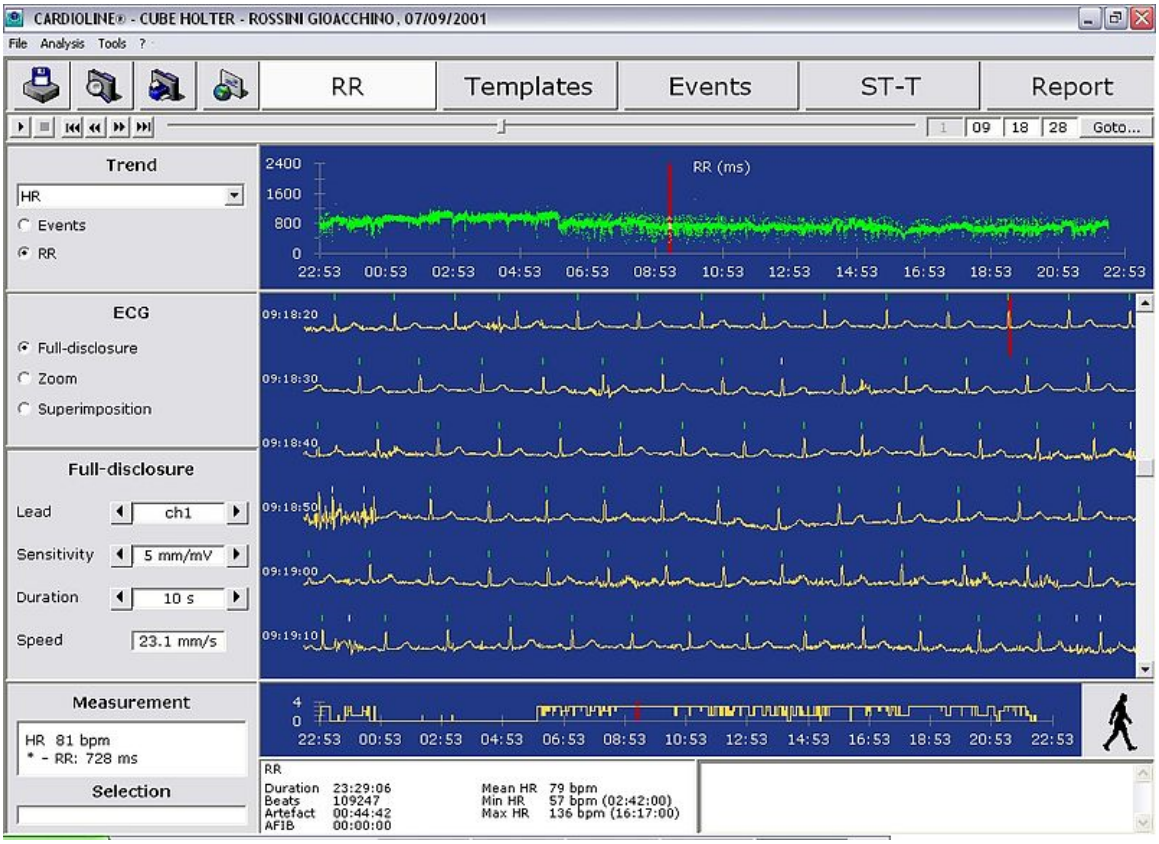
system, thus producing the signal in the same representation as during the common rest ECG and/or stress test measurement. These Holters then allow to substitute stress test examination in cases the stress test is not possible for the current patient. They are also suitable when analyzing patients after myocardial infarction. Recordings from these 12 lead monitors are of a significantly lower resolution than those from a standard 12 lead ECG and in some cases have been shown to provide misleading ST segment representation, even though some device allow to set the sampling frequency up to 1000 Hz for special purposes exams like the late potential.

Another interesting innovation is the presence of a 3 axis movement sensor, which record the patient physical activity, and later show in the software three different status: sleep, stand-up, walking. This helps the cardiologist to better analyze the recorded events belong to the patient activity and diary.

Analysing software

When the recording of ECG signal is finished (usually after 24 or 48 hours), it is up to the physician to perform the signal analysis. Since it would be extremely time demanding to browse through such a long signal, there is an integrated automatic analysis process in each Holter software which automatically determines different sorts of heart beats, rhythms, etc. However the success of the automatic analysis is very closely associated with the signal quality. The quality itself mainly depends on the attachment of the electrodes to the patient body. If these are not properly attached, the electromagnetic disturbance surrounding us will influence the ECG signal resulting thus in a very noisy record. If the patient moves rapidly, the distortion will be even bigger. Such record is then very difficult to process. Besides the attachment and quality of electrodes, there are other factors affecting the signal quality, such as muscle tremors, sampling rate and resolution of the digitized signal (high quality devices offer 2000Hz and 16 bits or higher).

The automatic analysis commonly provides the physician with information about heart beat morphology, beat interval measurement, heart rate variability, rhythm overview and patient diary (moments when the patient pressed the patient button). Advanced systems also perform spectral analysis, ischemic burden evaluation, graph of patient's activity or PQ segment analysis. Another requirement is the ability of pacemaker detection and analysis. Such ability is useful when one wants to check the correct pacemaker function.



Screenshot of an holter ecg software.

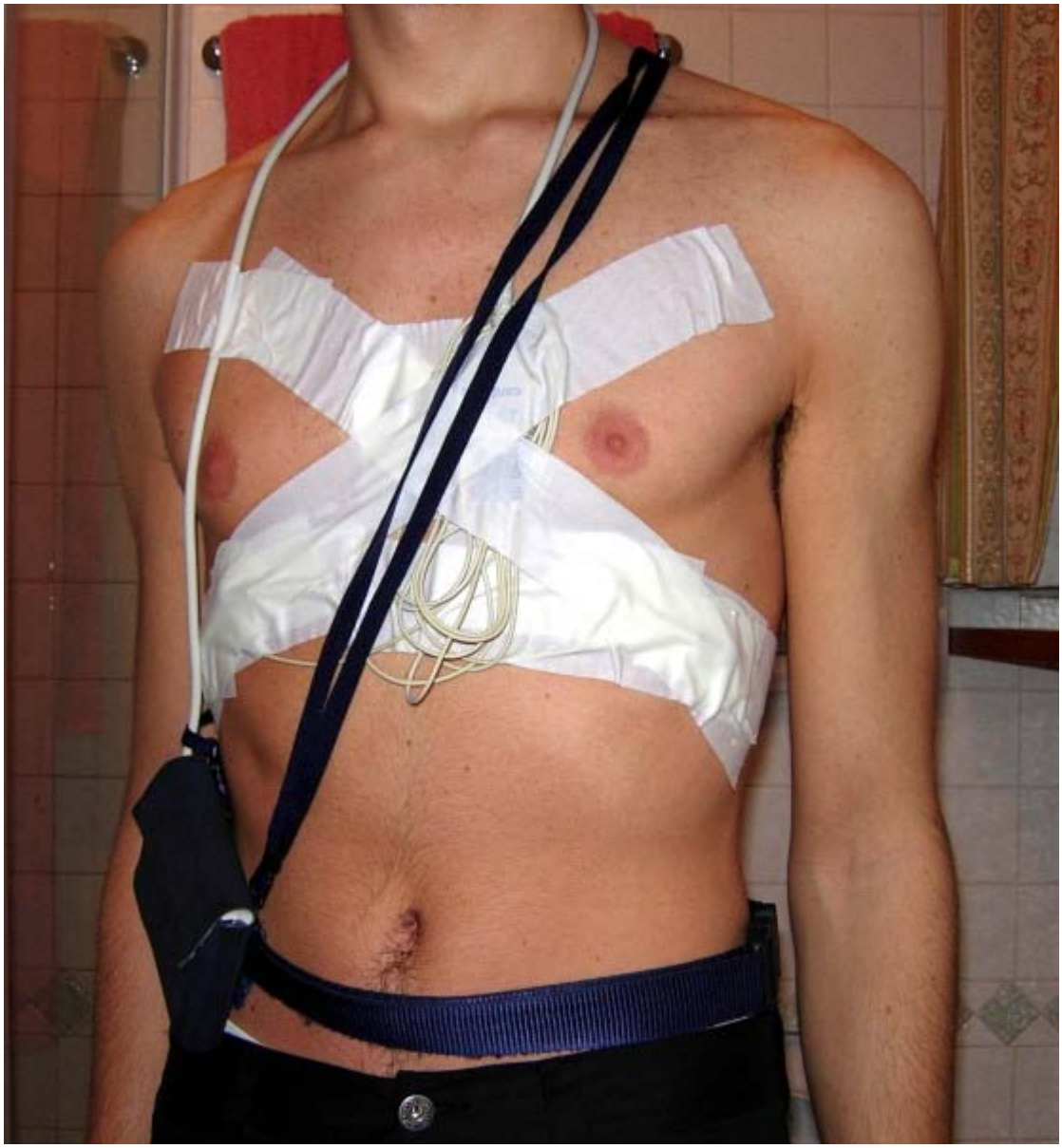
Wearing the monitor

Although some patients may feel uncomfortable about a Holter examination, there is nothing to worry about. No hazards are involved, and it should have little effect on one's normal daily life.

The recording device can be worn in a case on a belt or on a strap across the chest. The device may be visible under light clothing, and those wearing a Holter monitor may wish to avoid shirts with a low neckline.

Persons being monitored should not limit normal daily activities, since its purpose is to record how a heart works under various actual conditions over an extended period. It is an electrical device, however, and should be kept dry; showering or swimming should probably be avoided. Monitors can be removed for a few minutes without invalidating collected data, but proper reattachment is critical to avoid degradation of its signals. Beyond changing batteries, one should leave its handling to trained personnel.

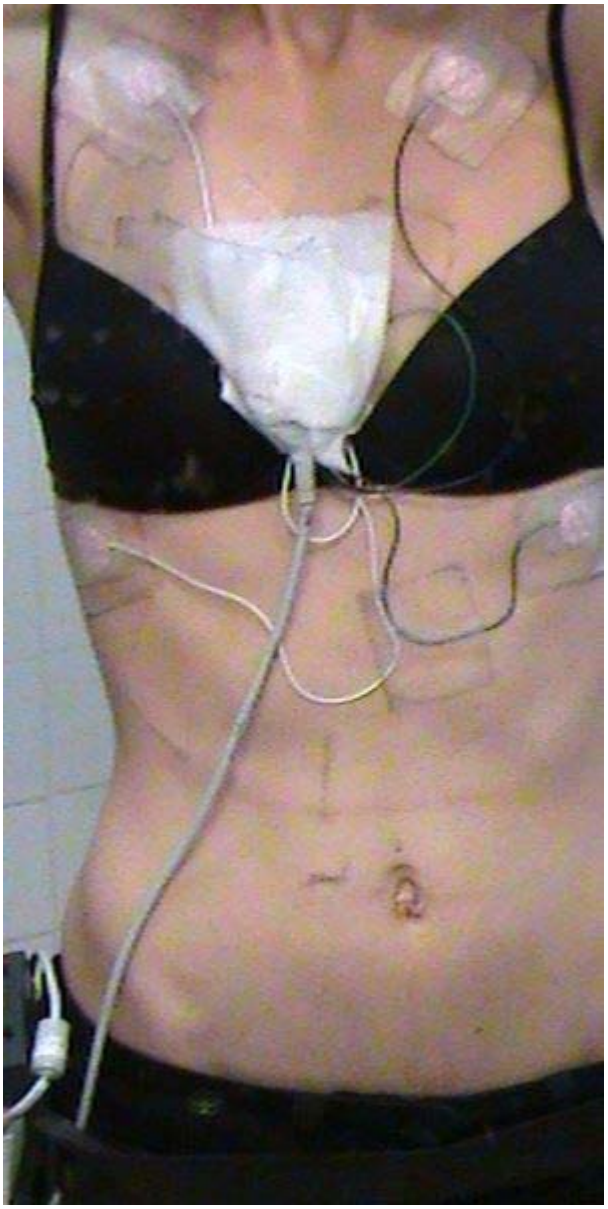
Gallery



A Holter monitor can be worn for many days without causing significant discomfort.

Canine Holter Monitor with DogLeggs Vest

A Holter monitor with a US quarter dollar coin to show scale



Holter monitor can be worn with bra on woman, with no discomfort.

Chapter 10

Laboratory Information System

A **lab information system** ("LIS") is a class of software that receives, processes, and stores information generated by medical laboratory processes. These systems often must interface with instruments and other information systems such as hospital information systems (HIS). A LIS is a highly configurable application which is customized to facilitate a wide variety of laboratory workflow models. Deciding on an LIS vendor is a major undertaking for all labs. Vendor selection typically takes months of research and planning. Installation takes from a few months to a few years depending on the complexity of the organization. There are as many variations of LISs as there are types of lab work. Some vendors offer a full-service solution capable of handling a large hospital lab's needs; others specialize in specific modules. Disciplines of laboratory science supported by LISs include hematology, chemistry, immunology, blood bank (Donor and Transfusion Management), surgical pathology, anatomical pathology, flow cytometry and microbiology.

Basic operation

Laboratory Information Systems are often part of an integrated informatics solution which involves many disparate applications. Use of an LIS is a critical piece of the clinical IT spectrum of systems and contributes significantly to the overall care given to patients. The LIS is used in inpatient and outpatient settings and in many cases is designed to support both. From an outpatient/ambulatory perspective, LIS interaction frequently begins after a physician has arrived at an initial diagnosis. For example, a patient enters the hospital looking pale and complaining of fatigue. The physician, suspecting anemia, might decide to order a complete blood count (CBC). In an inpatient setting when that patient is admitted into the hospital, the system is used to order tests, provide specimen processing assistance, receive the results from analyzers and deliver lab reports to the attending physician.

Order entry and check in

An order is placed in the system usually by a physician or laboratory scientist. The order or lab request contains a list of tests to be performed on one or more patient specimens

(e.g., blood or urine). In many cases, each order is tracked with a unique identifier. This identifier (which is usually a number) is often referred to as Lab ID. In this hypothetical case, a CBC is ordered which is a panel of sub-tests including white blood cell count, red cell blood count and other blood-related tests.

A phlebotomist will be called on to collect the specimen(s) from the patient. Often, different specimens will be collected, so as to provide different tubes (each with a specific cap color) for each analyzer that will process the samples. In this case, the appropriate specimen (using a vacutainer tube with a lavender top) is taken from the patient and labeled with a bar code specimen label produced by the LIS. The LIS will print barcode labels (with the unique lab ID) for the draw tubes. In some cases, more advanced LIS products will also provide a unique identifier for each specimen. This provides the ability to track the specimen's chain of custody from the point it is taken from the patient to the point that it gets discarded. The specimen-accession-patient hierarchy is linked in a tree like numeric structure. In other cases,the patient is identified by a Lab ID linked to the patient's demographic record through the Hospital number.

Specimen receiving

After the specimen is collected, it is sent/brought to the lab for processing typically in a batch. This event should be recorded in the LIS. On reception of the specimen in the testing lab, either manual or automated lab work can begin. Many tests, such as CBCs or Chemistry profiles, are performed by automated analyzers.

Send test orders to analyzers

Most LIS systems can be configured to download the specimen data to an analyzer either after the order is placed or when a specimen is received in a testing lab. When the specimen's barcode is read by the instrument, the unique ID from the specimen label is matched with the order previously downloaded to the instrument. This system is often called "Batch Download". A more efficient system is called "Host Query", where the instrument reads the barcode on the specimen and "queries" the LIS for the test orders. The LIS will be listening on a communication port for queries and will download the requests only when required. In cases where the LIS transmits data such as test orders or control messages to analyzers the communication is set up to be bi-directional.

Results entry

When results of lab tests are available, they are entered into the system manually or automatically downloaded from an instrument. Once these results are double-checked by the Medical Laboratory Scientist or autoverified, they are released. Released results are often automatically printed or written on lab reports which are delivered to the attending physician or clinic. Results must be verified and released to attending physicians as soon as possible.

Lab reporting

Lab Reports are the final output of all LIS systems and, in many cases, the primary LIS interaction with healthcare professionals outside the lab. The reports can either be printed or faxed in paper-based labs; they can be delivered via email or file in paperless labs. The degree to which an LIS supports customizable lab reports and flexibility in modes of delivery of results is one major factor in determining its success in the marketplace.

Basic features

Laboratory Information Systems commonly support the following features:

- Patient Check In
- Order Entry
- Specimen Processing
- Result(s) Entry
- Reporting
- Patient Demographics
- Physician Demographics

Additional features

In addition LISs commonly support the following:

- Web-based order entry
- Web-based results inquiry
- Faxing and emailing of lab reports
- Custom report creation
- HL7 interfaces with reference labs and EMRs
- Preliminary reporting
- Final reporting
- Med tech worksheets
- Workload balancing
- Medicare medical necessity checking
- Billing
- Public health reporting
- Rule engines
- report check by reputed pathologist and senior technologist

Types

There are many laboratory disciplines requiring the support of computerized informatics. These include:

- Hematology
- Chemistry

- Immunology
- Blood bank donor center
- Blood bank transfusion
- Surgical Pathology
- Pathology
- Cytology (Cytopathology)
- Microbiology
- Flow cytometry
- TB

Chapter 11

Medical Device

A **medical device** is a product which is used for medical purposes in patients, in diagnosis, therapy or surgery. Whereas *medicinal products* (also called *pharmaceuticals*) achieve their principal action by pharmacological, metabolic or immunological means. *Medical devices* act by other means like physical, mechanical, physico-chemical or chemical means. *Medical devices* are included in the category: *Medical technology*.

Medical devices include a wide range of products varying in complexity and application. Examples include tongue depressors, medical thermometers, blood sugar meters, total artificial hearts, fibrin scaffolds, stents and X-ray machines.

The global market of medical devices reached roughly 209 billion US Dollar in 2006 and is expected to grow with an average annual rate of 6 - 9% through 2010.

Definitions

European Union legal framework and definition

Based on the "New Approach", rules relating to the safety and performance of medical devices were harmonised in the EU in the 1990s. The "New Approach", defined in a European Council Resolution of May 1985, represents an innovative way of technical harmonisation. It aims to remove technical barriers to trade and dispel the consequent uncertainty for economic operators allowing for the free movement of goods inside the EU.

The core legal framework consists of 3 directives:

- Directive 90/385/EEC regarding active implantable medical devices;
- Directive 93/42/EEC regarding medical devices;
- Directive 98/79/EC regarding in vitro diagnostic medical devices.

They aim at ensuring a high level of protection of human health and safety and the good functioning of the Single Market. These 3 main directives have been supplemented over

time by several modifying and implementing directives, including the last technical revision brought about by Directive 2007/47 EC.

Directive 2007/47/ec defines a medical device as: *"any instrument, apparatus, appliance, software, material or other article, whether used alone or in combination, including the software intended by its manufacturer to be used specifically for diagnostic and/or therapeutic purposes and necessary for its proper application, intended by the manufacturer to be used for human beings. Devices are to be used for the purpose of:*

- Diagnosis, prevention, monitoring, treatment or alleviation of disease.
- Diagnosis, monitoring, treatment, alleviation of or compensation for an injury or handicap.
- Investigation, replacement or modification of the anatomy or of a physiological process
- Control of conception

This includes devices that do not achieve its principal intended action in or on the human body by pharmacological, immunological or metabolic means, but which may be assisted in its function by such means."

The government of each Member State is required to appoint a **Competent Authority** responsible for medical devices. The Competent Authority (CA) is a body with authority to act on behalf of the government of the Member State to ensure that the requirements of the Medical Device Directives are transposed into National Law and are applied. The Competent Authority reports to the Minister of Health in the Member State. • The Competent Authority in one Member State does not have jurisdiction in any other Member State, but they do exchange information and try to reach common positions.

In UK the Medicines and Healthcare products Regulatory Agency (MHRA) acts as a CA, in Italy it is the Ministero Salute (Ministry of Health)

Medical devices must not be mistaken with medicinal products. In the EU, all medical devices must be identified with the CE mark.

Definition in USA by the Food and Drug Administration

A medical device, according to the U.S. Food and Drug Administration (FDA): A device is an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes.

Definition in Canada by the Food and Drugs Act

The term medical devices, as defined in the Food and Drugs Act, covers a wide range of health or medical instruments used in the treatment, mitigation, diagnosis or prevention of a disease or abnormal physical condition. Health Canada reviews medical devices to assess their safety, effectiveness and quality before being authorized for sale in Canada.

Classification

The regulatory authorities recognize different classes of medical devices, based on their design complexity, their use characteristics, and their potential for harm if misused. Each country or region defines these categories in different ways. The authorities also recognize that some devices are provided in combination with drugs, and regulation of these combination products takes this factor into consideration.

Canada

The Medical Devices Bureau of Health Canada has recognized four classes of medical devices based on the level of control necessary to assure the safety and effectiveness of the device. Class I devices present the lowest potential risk and do not require a licence. Class II devices require the manufacturer's declaration of device safety and effectiveness, whereas Class III and IV devices present a greater potential risk and are subject to in-depth scrutiny. . A guidance document for device classification is published by Heath Canada .

Canadian classes of medical devices generally correspond to the European Council Directive 93/42/EEC (MDD) devices as follows: Class IV (Canada) generally corresponds to Class III (ECD), Class III (Canada) generally corresponds to Class IIb (ECD), Class II (Canada) generally corresponds to Class IIa (ECD), and Class I (Canada) generally corresponds to Class I (ECD) . Examples are surgical instruments (Class I); contact lenses, ultrasound scanners (Class II); orthopedic implants, hemodialysis machines (Class III); and cardiac pacemakers (Class IV) .

United States

The Food and Drug Administration has recognized three classes of medical devices based on the level of control necessary to assure the safety and effectiveness of the device. The classification procedures are described in the Code of Federal Regulations, Title 21, part 860 (usually known as 21 CFR 860).

Class I: General controls

Class I devices are subject to the least regulatory control. Class I devices are subject to "General Controls" as are Class II and Class III devices. General controls include provisions that relate to adulteration; misbranding; device registration and listing; premarket notification; banned devices; notification, including repair, replacement, or

refund; records and reports; restricted devices; and good manufacturing practices. Class I devices are not intended for use in supporting or sustaining life or to be of substantial importance in preventing impairment to human health, and they may not present a potential unreasonable risk of illness or injury. Most Class I devices are exempt from the premarket notification and/or good manufacturing practices regulation. Examples of Class I devices include elastic bandages, examination gloves, and hand-held surgical instruments.

Class II: General controls with special controls

Class II devices are those for which general controls alone are insufficient to assure safety and effectiveness, and existing methods are available to provide such assurances. In addition to complying with general controls, Class II devices are also subject to special controls. A few Class II devices are exempt from the premarket notification. Special controls may include special labeling requirements, mandatory performance standards and postmarket surveillance. Devices in Class II are held to a higher level of assurance than Class I devices, and are designed to perform as indicated without causing injury or harm to patient or user. Examples of Class II devices include powered wheelchairs, infusion pumps, and surgical drapes.

Class III: general controls and premarket approval

A Class III device is one for which insufficient information exists to assure safety and effectiveness solely through the general or special controls sufficient for Class I or Class II devices. Such a device needs premarket approval, a scientific review to ensure the device's safety and effectiveness, in addition to the general controls of Class I. Class III devices are usually those that support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury. Examples of Class III devices which currently require a premarket notification include implantable pacemaker, pulse generators, HIV diagnostic tests, automated external defibrillators, and endosseous implants.

European Union (EU) and European Free Trade Association (EFTA)

The classification of medical devices in the European Union is outlined in Annex IX of the Council Directive 93/42/EEC. There are basically four classes, ranging from low risk to high risk.

- Class I (including Is & Im)
- Class IIa
- Class IIb
- Class III

The authorization of medical devices is guaranteed by a Declaration of Conformity. This declaration is issued by the manufacturer itself, but for products in Class Is, Im, IIa, IIb or III, it must be verified by a Certificate of Conformity issued by a Notified Body. A

Notified Body is a public or private organisation that has been accredited to validate the compliance of the device to the European Directive. Medical devices that pertain to class I (on condition they do not need to be sterilised or are not used to measure a function) can be put on the market purely by self-certification.

The European classification depends on rules that involve the medical device's duration of body contact, its invasive character, its use of an energy source, its effect on the central circulation or nervous system, its diagnostic impact or its incorporation of a medicinal product.

Certified medical devices should have the CE mark on the packaging, insert leaflets, etc.. These packagings should also show harmonised pictograms and EN standardised logos to indicate essential features such as instructions for use, expiry date, manufacturer, sterile, don't reuse, etc.

Radio-frequency identification

Medical devices incorporating RFID

In 2004, the FDA authorized marketing of two different types of medical devices that incorporate radio-frequency identification, or RFID. The first type is the SurgiChip tag, an external surgical marker that is intended to minimize the likelihood of wrong-site, wrong-procedure and wrong-patient surgeries. The tag consists of a label with passive transponder, along with a printer, an encoder and a RFID reader. The tag is labeled and encoded with the patient's name and the details of the planned surgery, and then placed in the patient's chart. On the day of surgery, the adhesive-backed tag is placed on the patient's body near the surgical site. In the operating room the tag is scanned and the information is verified with the patient's chart. Just before surgery, the tag is removed and placed back in the chart.

The second type of RFID medical device is the implantable radiofrequency transponder system for patient identification and health information. One example of this type of medical device is the VeriChip, which includes a passive implanted transponder, inserter and scanner. The chip stores a unique electronic identification code that can be used to access patient identification and corresponding health information in a database. The chip itself does not store health information or a patient's name.

Practical and information security considerations

Companies developing RFID-containing medical devices must consider product development issues common to other medical devices that come into contact with the body, are implanted in the body, or use computer software. For example, as part of product development, a company must implement controls and conduct testing on issues such as product performance, sterility, adverse tissue reactions, migration of the implanted transponder, electromagnetic interference, and software validation.

Medical devices that use RFID technology to store, access, and/or transfer patient information also raise significant issues regarding information security. The FDA defines "information security" as the process of preventing the modification, misuse or denial of use, or the unauthorized use of that information. At its core, this means ensuring the privacy of patient information.

Four components of information security

The FDA has recommended that a company's specifications for implantable RFID-containing medical devices address the following four components of information security: confidentiality, integrity, availability and accountability (CIAA).

- Confidentiality means data and information are disclosed only to authorized persons, entities and processes at authorized times and in the authorized manner. This ensures that no unauthorized users have access to the information.

- Integrity means data and information are accurate and complete, and the accuracy and completeness are preserved. This ensures that the information is correct and has not been improperly modified.

- Availability means data, information and information systems are accessible and usable on a timely basis in the required manner. This ensures that the information will be available when needed.

- Accountability is the application of identification and authentication to ensure that the prescribed access process is followed by an authorized user.

Although the FDA made these recommendations in the context of implantable RFID-containing medical devices, these principles are relevant to all uses of RFID in connection with pharmaceuticals and medical devices.

List of medical devices

High-risk devices

High-risk devices are life supports, critical monitoring, energy emitting and other devices whose failure or misuse is reasonably likely to seriously injure patient or staff. Examples include:

- Anesthesia units
- Anesthesia ventilators
- Apnea monitors
- Argon enhanced coagulation units
- Aspirators
- Auto transfusion units
- Cardiac defibrillator, external or internal

- Electrosurgical units
- External pacemaker
- Fetal monitors
- Heart-lung machine
- Incubators
- Infusion pump
- Invasive blood pressure units
- Pulse oximeters
- Radiation-therapy machines
- Ventilator
- Stent

An example of the stent used in an EVAR procedure

Medium-risk devices

These are devices including many diagnostic instruments whose misuse, failure or absence (e.g. out of service) with no replacement available would have a significant impact on patient care, but would not be likely to cause direct serious injury. Examples include:

- ECG
- EEG
- Treadmills
- Ultrasound sensors
- Phototherapy units
- Endoscopes
- Human-implantable RFID chips
- Surgical drill and saws
- Laparoscopic insufflators
- Phonocardiographs
- radiant warmers (adult)
- Zoophagous agents (e.g., medicinal leeches; medicinal maggots)
- Lytic bacteriophages

Low-risk devices

Devices in this category are those whose failure or misuse is unlikely to result in serious consequences. Examples include:

- Electronic thermometer,
- Breast pumps
- Surgical microscope
- Ultrasonic nebulizers
- Sphygmomanometers
- Surgical table
- Surgical lights.
- Temperature monitor
- Aspirators
- X-ray diagnostic equipment
- Lensometer
- keratometer

Standardization and regulatory concerns

The ISO standards for medical devices are covered by ICS 11.100.20 and 11.040.01 . The quality and risk management regarding the topic for regulatory purposes is convened by ISO 13485 and ISO 14971. Further standards are IEC 60601-1, for electrical devices (mains-powered as well as battery powered) and IEC 62304 for medical software. The

US FDA also published a series of guidances for industry regarding this topic against 21 CFR Subchapter H—Medical Devices.

Starting in the late 1980s the FDA increased its involvement in reviewing the development of medical device software. The precipitant for change was a radiation therapy device (Therac-25) that overdosed patients because of software coding errors.. FDA is now focused on regulatory oversight on medical device software development process and system-level testing.

Packaging standards

Medical device packaging is highly regulated. Often medical devices and products are sterilized in the package. The sterility must be maintained throughout distribution to allow immediate use by physicians. A series of special packaging tests is used to measure the ability of the package to maintain sterility. Relevant standards include: ASTM D1585- Guide for Integrity Testing of Porous Medical Packages, ASTM F2097- Standard Guide for Design and Evaluation of Primary Flexible Packaging for Medical Products , EN 868 Packaging materials and systems for medical devices which are to be sterilized. General requirements and test methods, ISO 11607 Packaging for terminally sterilized medical devices, and others.

Academic resources

- *Medical & Biological Engineering & Computing*
- *Expert Review of Medical Devices*
- *Journal of Clinical Engineering*

Chapter 12

Medical Imaging

Medical imaging is the technique and process used to create images of the human body (or parts and function thereof) for clinical purposes (medical procedures seeking to reveal, diagnose or examine disease) or medical science (including the study of normal anatomy and physiology). Although imaging of removed organs and tissues can be performed for medical reasons, such procedures are not usually referred to as medical imaging, but rather are a part of pathology.

As a discipline and in its widest sense, it is part of biological imaging and incorporates radiology (in the wider sense), nuclear medicine, investigative radiological sciences, endoscopy, (medical) thermography, medical photography and microscopy (e.g. for human pathological investigations).

Measurement and recording techniques which are not primarily designed to produce images, such as electroencephalography (EEG), magnetoencephalography (MEG), Electrocardiography (EKG) and others, but which produce data susceptible to be represented as maps (i.e. containing positional information), can be seen as forms of medical imaging.

Up until 2010, 5 billion medical imaging studies had been conducted worldwide. Radiation exposure from medical imaging in 2006 made up about 50% of total ionizing radiation exposure in the United States.

Overview

In the clinical context, "invisible light" medical imaging is generally equated to radiology or "clinical imaging" and the medical practitioner responsible for interpreting (and sometimes acquiring) the images is a radiologist. "Visible light" medical imaging involves digital video or still pictures that can be seen without special equipment. Dermatology and wound care are two modalities that utilize visible light imagery.

Diagnostic radiography designates the technical aspects of medical imaging and in particular the acquisition of medical images. The *radiographer* or *radiologic technologist* is usually responsible for acquiring medical images of diagnostic quality, although some radiological interventions are performed by radiologists. While radiology is an evaluation of anatomy, nuclear medicine provides functional assessment.

As a field of scientific investigation, medical imaging constitutes a sub-discipline of biomedical engineering, medical physics or medicine depending on the context: Research and development in the area of instrumentation, image acquisition (e.g. radiography), modelling and quantification are usually the preserve of biomedical engineering, medical physics and computer science; Research into the application and interpretation of medical images is usually the preserve of radiology and the medical sub-discipline relevant to medical condition or area of medical science (neuroscience, cardiology, psychiatry, psychology, etc.) under investigation. Many of the techniques developed for medical imaging also have scientific and industrial applications.

Medical imaging is often perceived to designate the set of techniques that noninvasively produce images of the internal aspect of the body. In this restricted sense, medical imaging can be seen as the solution of mathematical inverse problems. This means that cause (the properties of living tissue) is inferred from effect (the observed signal). In the case of ultrasonography the probe consists of ultrasonic pressure waves and echoes inside the tissue show the internal structure. In the case of projection radiography, the probe is X-ray radiation which is absorbed at different rates in different tissue types such as bone, muscle and fat.

The term noninvasive is a term based on the fact that following medical imaging modalities do not penetrate the skin physically. But on the electromagnetic and radiation level, they are quite invasive. From the high energy photons in X-Ray Computed Tomography, to the 2+ Tesla coils of an MRI device, these modalities alter the physical and chemical environment of the body in order to obtain data.

Imaging technology

Radiography

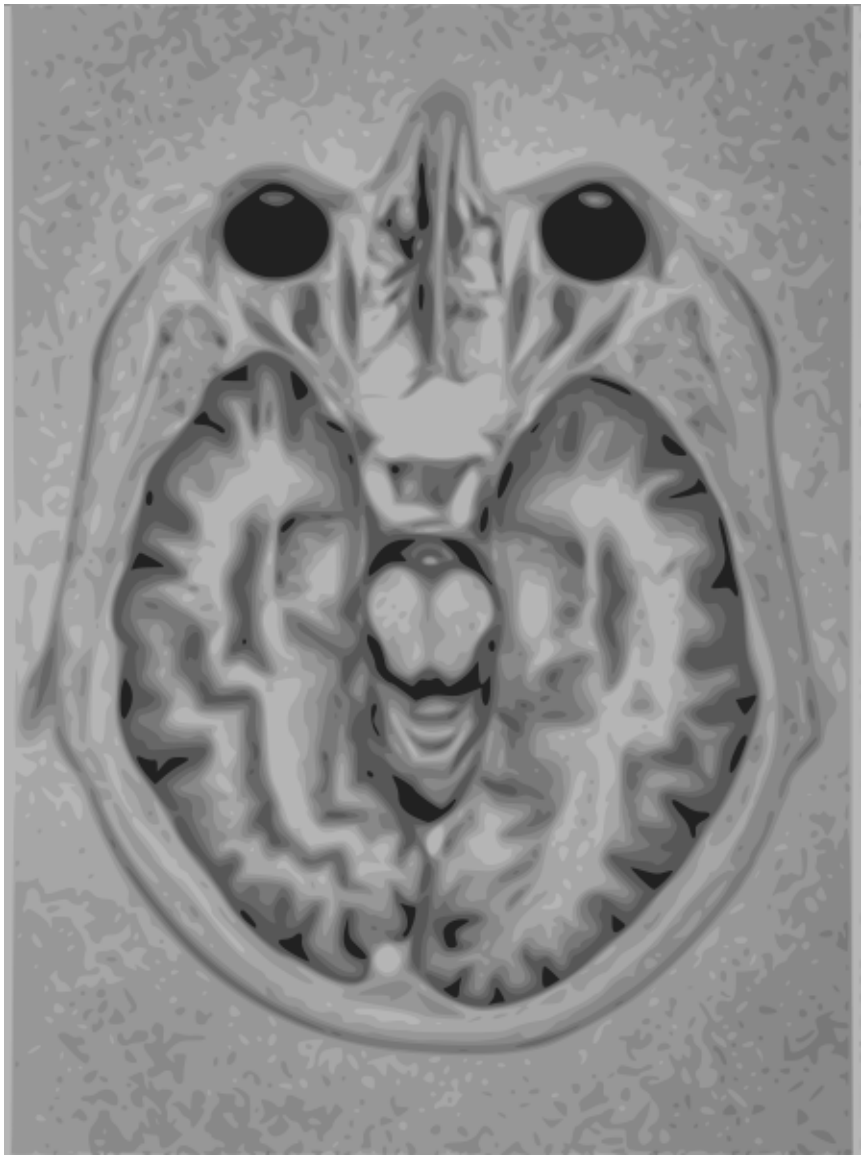
Two forms of radiographic images are in use in medical imaging; projection radiography and fluoroscopy, with the latter being useful for catheter guidance. These 2D techniques are still in wide use despite the advance of 3D tomography due to the low cost, high resolution, and depending on application, lower radiation dosages. This imaging modality utilizes a wide beam of x rays for image acquisition and is the first imaging technique available in modern medicine.

- *Fluoroscopy* produces real-time images of internal structures of the body in a similar fashion to radiography, but employs a constant input of x-rays, at a lower dose rate. Contrast media, such as barium, iodine, and air are used to visualize internal organs as they work. Fluoroscopy is also used in image-guided

procedures when constant feedback during a procedure is required. An image receptor is required to convert the radiation into an image after it has passed through the area of interest. Early on this was a fluorescing screen, which gave way to an Image Amplifier (IA) which was a large vacuum tube that had the receiving end coated with cesium iodide, and a mirror at the opposite end. Eventually the mirror was replaced with a TV camera.

- *Projectional radiographs*, more commonly known as x-rays, are often used to determine the type and extent of a fracture as well as for detecting pathological changes in the lungs. With the use of radio-opaque contrast media, such as barium, they can also be used to visualize the structure of the stomach and intestines - this can help diagnose ulcers or certain types of colon cancer.

Magnetic resonance imaging (MRI)



A brain MRI representation

A magnetic resonance imaging instrument (MRI scanner), or "nuclear magnetic resonance (NMR) imaging" scanner as it was originally known, uses powerful magnets to polarise and excite hydrogen nuclei (single proton) in water molecules in human tissue, producing a detectable signal which is spatially encoded, resulting in images of the body. MRI uses three electromagnetic fields: a very strong (on the order of units of teslas) static magnetic field to polarize the hydrogen nuclei, called the static field; a weaker time-varying (on the order of 1 kHz) field(s) for spatial encoding, called the gradient field(s); and a weak radio-frequency (RF) field for manipulation of the hydrogen nuclei to produce measurable signals, collected through an RF antenna.

Like CT, MRI traditionally creates a two dimensional image of a thin "slice" of the body and is therefore considered a tomographic imaging technique. Modern MRI instruments are capable of producing images in the form of 3D blocks, which may be considered a generalisation of the single-slice, tomographic, concept. Unlike CT, MRI does not involve the use of ionizing radiation and is therefore not associated with the same health hazards. For example, because MRI has only been in use since the early 1980s, there are no known long-term effects of exposure to strong static fields and therefore there is no limit to the number of scans to which an individual can be subjected, in contrast with X-ray and CT. However, there are well-identified health risks associated with tissue heating from exposure to the RF field and the presence of implanted devices in the body, such as pace makers. These risks are strictly controlled as part of the design of the instrument and the scanning protocols used.

Because CT and MRI are sensitive to different tissue properties, the appearance of the images obtained with the two techniques differ markedly. In CT, X-rays must be blocked by some form of dense tissue to create an image, so the image quality when looking at soft tissues will be poor. In MRI, while any nucleus with a net nuclear spin can be used, the proton of the hydrogen atom remains the most widely used, especially in the clinical setting, because it is so ubiquitous and returns a large signal. This nucleus, present in water molecules, allows the excellent soft-tissue contrast achievable with MRI.

Nuclear medicine

Nuclear medicine encompasses both diagnostic imaging and treatment of disease, and may also be referred to as molecular medicine or molecular imaging & therapeutics . Nuclear medicine uses certain properties of isotopes and the energetic particles emitted from radioactive material to diagnose or treat various pathology. Different from the typical concept of anatomic radiology, nuclear medicine enables assessment of physiology. This function-based approach to medical evaluation has useful applications in most subspecialties, notably oncology, neurology, and cardiology. *Gamma cameras* are used in e.g. scintigraphy, SPECT and PET to detect regions of biologic activity that may be associated with disease. Relatively short lived isotope, such as ^{123}I is administered to the patient. Isotopes are often preferentially absorbed by biologically active tissue in the body, and can be used to identify tumors or fracture points in bone. Images are acquired after collimated photons are detected by a crystal that gives off a light signal, which is in turn amplified and converted into count data.

- *Scintigraphy* ("scint") is a form of diagnostic test wherein radioisotopes are taken internally, for example intravenously or orally. Then, gamma cameras capture and form two-dimensional images from the radiation emitted by the radiopharmaceuticals.
- *SPECT* is a 3D tomographic technique that uses gamma camera data from many projections and can be reconstructed in different planes. A dual detector head gamma camera combined with a CT scanner, which provides localization of functional SPECT data, is termed a SPECT/CT camera, and has shown utility in advancing the field of molecular imaging. In most other medical imaging modalities, energy is passed through the body and the reaction or result is read by detectors. In SPECT imaging, the patient is injected with a radioisotope, most commonly Thallium 201TI, Technetium 99mTC, Iodine 123I, and Gallium 67Ga

The radioactive gamma rays are emitted through the body as the natural decaying process of these isotopes takes place. The emissions of the gamma rays are captured by detectors that surround the body. This essentially means that the human is now the source of the radioactivity, rather than the medical imaging devices such as X-Ray, CT, or Ultrasound.

- *Positron emission tomography* (PET) uses coincidence detection to image functional processes. Short-lived positron emitting isotope, such as ^{18}F, is incorporated with an organic substance such as glucose, creating F18-fluorodeoxyglucose, which can be used as a marker of metabolic utilization. Images of activity distribution throughout the body can show rapidly growing tissue, like tumor, metastasis, or infection. PET images can be viewed in comparison to computed tomography scans to determine an anatomic correlate. Modern scanners combine PET with a CT, or even MRI, to optimize the image reconstruction involved with positron imaging. This is performed on the same equipment without physically moving the patient off of the gantry. The resultant hybrid of functional and anatomic imaging information is a useful tool in non-invasive diagnosis and patient management.

Photo acoustic imaging

Photoacoustic imaging is a recently developed hybrid biomedical imaging modality based on the photoacoustic effect. It combines the advantages of optical absorption contrast with ultrasonic spatial resolution for deep imaging in (optical) diffusive or quasi-diffusive regime. Recent studies have shown that photoacoustic imaging can be used in vivo for tumor angiogenesis monitoring, blood oxygenation mapping, functional brain imaging, and skin melanoma detection, etc.

Breast Thermography

Digital infrared imaging thermography is based on the principle that metabolic activity and vascular circulation in both pre-cancerous tissue and the area surrounding a developing breast cancer is almost always higher than in normal breast tissue. Cancerous tumors require an ever-increasing supply of nutrients and therefore increase circulation to

their cells by holding open existing blood vessels, opening dormant vessels, and creating new ones (neoangiogenesis). This process frequently results in an increase in regional surface temperatures of the breast. Digital infrared imaging uses extremely sensitive medical infrared cameras and sophisticated computers to detect, analyze, and produce high-resolution diagnostic images of these temperature variations. Because of DII's sensitivity, these temperature variations may be among the earliest signs of breast cancer and/or a pre-cancerous state of the breast.

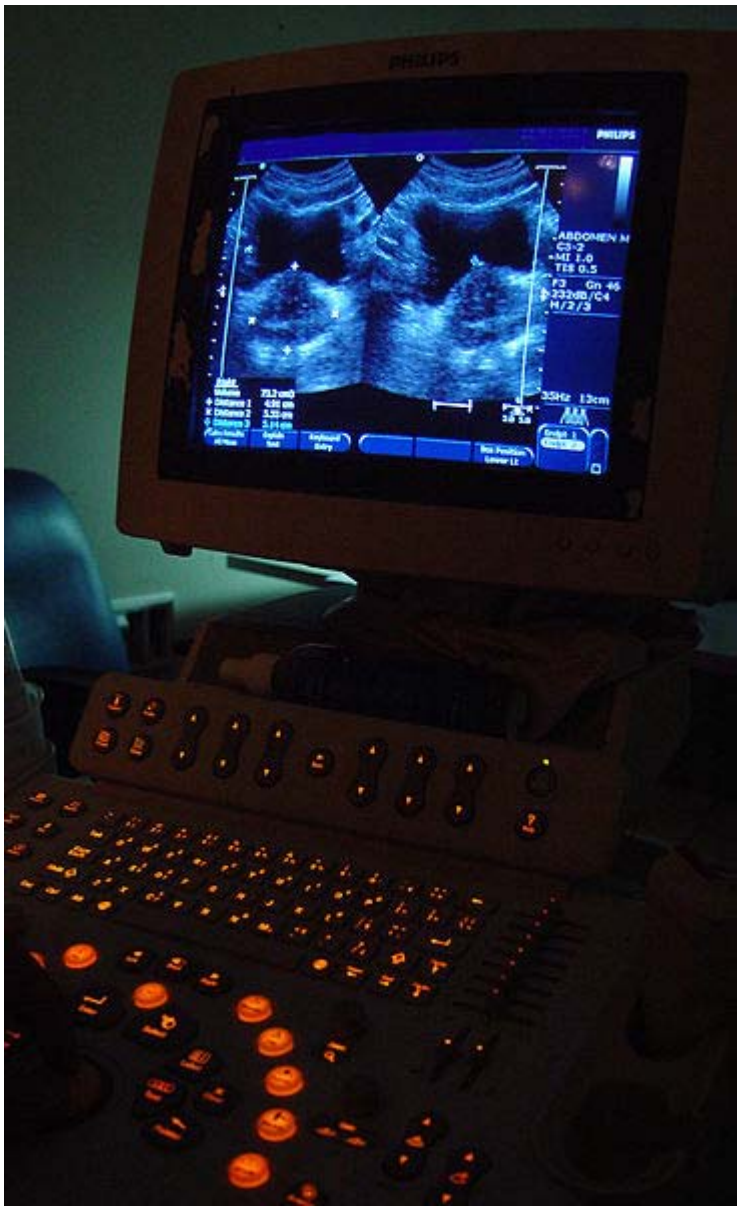
Tomography

Tomography is the method of imaging a single plane, or slice, of an object resulting in a tomogram. There are several forms of tomography:

- Linear tomography: This is the most basic form of tomography. The X-ray tube moved from point "A" to point "B" above the patient, while the cassette holder (or "bucky") moves simultaneously under the patient from point "B" to point "A." The fulcrum, or pivot point, is set to the area of interest. In this manner, the points above and below the focal plane are blurred out, just as the background is blurred when panning a camera during exposure. No longer carried out and replaced by computed tomography.
- Poly tomography: This was a complex form of tomography. With this technique, a number of geometrical movements were programmed, such as hypocycloidic, circular, figure 8, and elliptical. Philips Medical Systems produced one such device called the 'Polytome.' This unit was still in use into the 1990s, as its resulting images for small or difficult physiology, such as the inner ear, was still difficult to image with CTs at that time. As the resolution of CTs got better, this procedure was taken over by the CT.
- Zonography: This is a variant of linear tomography, where a limited arc of movement is used. It is still used in some centres for visualising the kidney during an intravenous urogram (IVU).
- Orthopantomography (OPT or OPG): The only common tomographic examination in use. This makes use of a complex movement to allow the radiographic examination of the mandible, as if it were a flat bone. It is often referred to as a "Panorex", but this is incorrect, as it is a trademark of a specific company.
- Computed Tomography (CT), or Computed Axial Tomography (CAT: A CT scan, also known as a CAT scan), is a helical tomography (latest generation), which traditionally produces a 2D image of the structures in a thin section of the body. It uses X-rays. It has a greater ionizing radiation dose burden than projection radiography; repeated scans must be limited to avoid health effects. CT is based on the same principles as X-Ray projections but in this case, the patient is enclosed in a surrounding ring of detectors assigned with 500-1000 scintillation detectors

This being the fourth-generation X-Ray CT scanner geometry. Previously in older generation scanners, the X-Ray beam was paired by a translating source and detector.

Ultrasound



Ultrasound representation of Urinary bladder (black butterfly-like shape) and hyperplastic prostate

Medical ultrasonography uses high frequency broadband sound waves in the megahertz range that are reflected by tissue to varying degrees to produce (up to 3D) images. This is commonly associated with imaging the fetus in pregnant women. Uses of ultrasound are much broader, however. Other important uses include imaging the abdominal organs, heart, breast, muscles, tendons, arteries and veins. While it may provide less anatomical detail than techniques such as CT or MRI, it has several advantages which make it ideal in numerous situations, in particular that it studies the function of moving structures in real-time, emits no ionizing radiation, and contains speckle that can be used in elastography. Ultrasound is also used as a popular research tool for capturing raw data,

that can be made available through an Ultrasound research interface, for the purpose of tissue characterization and implementation of new image processing techniques. The concepts of ultrasound differ from other medical imaging modalities in the fact that it is operated by the transmission and receipt of sound waves. The high frequency sound waves are sent into the tissue and depending on the composition of the different tissues; the signal will be attenuated and returned at separate intervals. A path of reflected sound waves in a multilayered structure can be defined by an input acoustic impedance(Ultrasound sound wave) and the Reflection and transmission coefficients of the relative structures . It is very safe to use and does not appear to cause any adverse effects, although information on this is not well documented. It is also relatively inexpensive and quick to perform. Ultrasound scanners can be taken to critically ill patients in intensive care units, avoiding the danger caused while moving the patient to the radiology department. The real time moving image obtained can be used to guide drainage and biopsy procedures. Doppler capabilities on modern scanners allow the blood flow in arteries and veins to be assessed.

Medical imaging topics

Maximizing imaging procedure use

The amount of data obtained in a single MR or CT scan is very extensive. Some of the data that radiologists discard could save patients time and money, while reducing their exposure to radiation and risk of complications from invasive procedures.

Creation of three-dimensional images

Recently, techniques have been developed to enable CT, MRI and ultrasound scanning software to produce 3D images for the physician. Traditionally CT and MRI scans produced 2D static output on film. To produce 3D images, many scans are made, then combined by computers to produce a 3D model, which can then be manipulated by the physician. 3D ultrasounds are produced using a somewhat similar technique. In diagnosing disease of the viscera of abdomen,ultrasound is particularly sensitive on imaging of biliary tract,urinary tract and female reproductive organs (ovary,fallopian tubes). As for example,diagnosis of gall stone by dilatation of common bile duct and stone in common bile duct . With the ability to visualize important structures in great detail, 3D visualization methods are a valuable resource for the diagnosis and surgical treatment of many pathologies. It was a key resource for the famous, but ultimately unsuccessful attempt by Singaporean surgeons to separate Iranian twins Ladan and Laleh Bijani in 2003. The 3D equipment was used previously for similar operations with great success.

Other proposed or developed techniques include:

- Diffuse optical tomography
- Elastography
- Electrical impedance tomography

- Optoacoustic imaging
- Ophthalmology
    - A-scan
    - B-scan
    - Corneal topography
    - Optical coherence tomography
    - Scanning laser ophthalmoscopy

Some of these techniques are still at a research stage and not yet used in clinical routines.

Compression of medical images

Medical imaging techniques produce very large amounts of data, especially from CT, MRI and PET modalities. As a result, storage and communications of electronic image data are prohibitive without the use of compression. JPEG 2000 is the state-of-the-art image compression DICOM standard for storage and transmission of medical images. The cost and feasibility of accessing large image data sets over low or various bandwidths are further addressed by use of another DICOM standard, called JPIP, to enable efficient streaming of the JPEG 2000 compressed image data.

Non-diagnostic imaging

Neuroimaging has also been used in experimental circumstances to allow people (especially disabled persons) to control outside devices, acting as a brain computer interface.

Archiving and recording

Used primarily in ultrasound imaging, capturing the image a medical imaging device is required for archiving and telemedicine applications. In most scenarios, a frame grabber is used in order to capture the video signal from the medical device and relay it to a computer for further processing and operations.

Open source software for medical image analysis

Several open source software packages are available for performing analysis of medical images:

- ImageJ
- 3D Slicer
- ITK
- OsiriX
- GemIdent
- MicroDicom
- FreeSurfer

Use in pharmaceutical clinical trials

Medical imaging has become a major tool in clinical trials since it enables rapid diagnosis with visualization and quantitative assessment.

A typical clinical trial goes through multiple phases and can take up to eight years. Clinical endpoints or outcomes are used to determine whether the therapy is safe and effective. Once a patient reaches the endpoint, he/she is generally excluded from further experimental interaction. Trials that rely solely on clinical endpoints are very costly as they have long durations and tend to need large number of patients.

In contrast to clinical endpoints, surrogate endpoints have been shown to cut down the time required to confirm whether a drug has clinical benefits. Imaging biomarkers (a characteristic that is objectively measured by an imaging technique, which is used as an indicator of pharmacological response to a therapy) and surrogate endpoints have shown to facilitate the use of small group sizes, obtaining quick results with good statistical power.

Imaging is able to reveal subtle change that is indicative of the progression of therapy that may be missed out by more subjective, traditional approaches. Statistical bias is reduced as the findings are evaluated without any direct patient contact.

For example, measurement of tumour shrinkage is a commonly used surrogate endpoint in solid tumour response evaluation. This allows for faster and more objective assessment of the effects of anticancer drugs. In evaluating the extent of Alzheimer's disease, it is still prevalent to use behavioural and cognitive tests. MRI scans on the entire brain can accurately pinpoint hippocampal atrophy rate while PET scans is able to measure the brain's metabolic activity by measuring regional glucose metabolism.

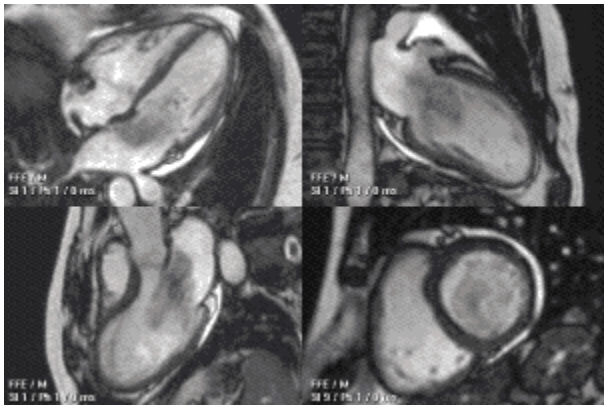
An imaging-based trial will usually be made up of three components:

1. A realistic imaging protocol. The protocol is an outline that standardizes (as far as practically possible) the way in which the images are acquired using the various modalities (PET, SPECT, CT, MRI). It covers the specifics in which images are to be stored, processed and evaluated.
2. An imaging centre that is responsible for collecting the images, perform quality control and provide tools for data storage, distribution and analysis. It is important for images acquired at different time points are displayed in a standardised format to maintain the reliability of the evaluation. Certain specialised imaging contract research organizations provide to end medical imaging services, from protocol design and site management through to data quality assurance and image analysis.
3. Clinical sites that recruit patients to generate the images to send back to the imaging centre.

Chapter 13

Cardiovascular Magnetic Resonance Imaging

Cardiovascular magnetic resonance imaging (CMR), sometimes known as **cardiac MRI**, is a medical imaging technology for the non-invasive assessment of the function and structure of the cardiovascular system. It is derived from and based on the same basic principles as magnetic resonance imaging (MRI) but with optimisation for use in the cardiovascular system. These optimisations are principally in the use of ECG gating and rapid imaging techniques or sequences. By combining a variety of such techniques into protocols, key functional and morphological features of the cardiovascular system can be assessed.



History and nomenclature

The phenomenon of nuclear magnetic resonance (NMR) was first described in molecular beams (1938) and bulk matter (1946), work later acknowledged by the award of a joint Nobel prize in 1952. Further investigation laid out the principles of relaxation times leading to nuclear spectroscopy. In 1973, the first simple NMR image was published and the first medical imaging in 1977, entering the clinical arena in the early 1980s. In 1984, NMR medical imaging was renamed MRI. Initial attempts to image the heart were confounded by respiratory and cardiac motion, solved by using cardiac ECG gating,

faster scan techniques and breath hold imaging. Increasingly sophisticated techniques were developed including cine imaging and techniques to characterise heart muscle as normal or abnormal (fat infiltration, oedematous, iron loaded, acutely infarcted or fibrosed).

As MRI became more complex and application to cardiovascular imaging became more sophisticated, the Society for Cardiovascular Magnetic Resonance, SCMR was set up (1996) with an academic journal, (JCMR) in 1999, which is going open source in 2008. In a move analogous to the development of 'echocardiography' from cardiac ultrasound, the term 'Cardiovascular Magnetic Resonance' (CMR) was proposed and has gained acceptance as the name for the field.

Physics

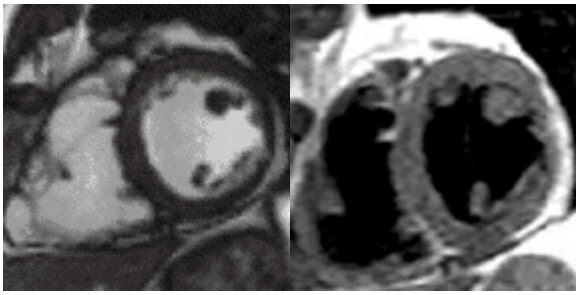
CMR uses the same basic principles as other MRI techniques with the addition of ECG gating. Most CMR uses only ^{1}H nuclei MR, which are abundant in human tissue. By using magnetic fields and radiofrequency (RF) pulses, the patient's own ^{1}H nuclei absorb and then emit energy, which can be measured and translated into images, without using ionising radiation.

Techniques

CMR uses several different techniques within a single scan. The combination of these results in a comprehensive assessment of the heart and cardiovascular system. Examples are below:

Visualising heart muscle scar or fat without using a contrast agent

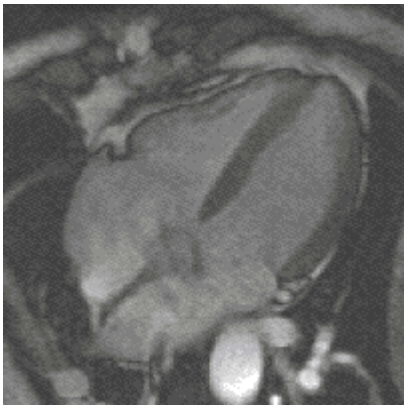
Typically a sequence called spin-echo is used. This causes the blood to appear black. These are high resolution still images which in certain circumstances identify abnormal myocardium through differences in intrinsic contrast.



Heart function using cine imaging

Images of the heart may be acquired in real-time with CMR, but the image quality is limited. Instead most sequences use ECG gating to acquire images at each stage of the cardiac cycle over several heart beats. This technique forms the basis of functional

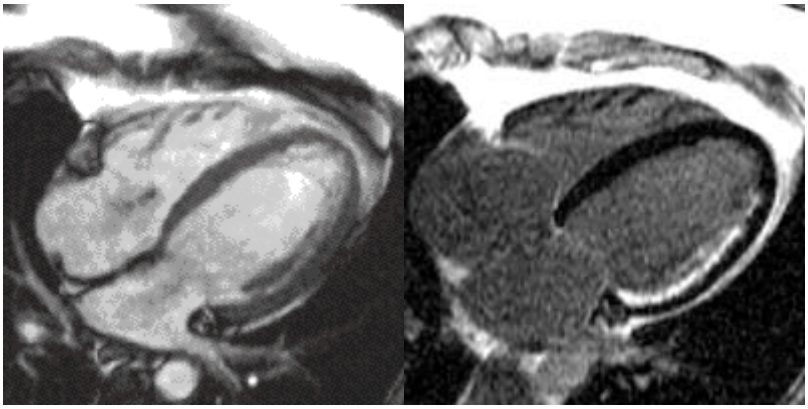
assessment by CMR. Blood typically appears bright in these sequences due to the contrast properties of blood and its rapid flow. The technique can discriminate very well between blood and myocardium. The current technique typically used for this is called balanced steady state free precession (SSFP), implemented as TrueFISP, b-FFE or Fiesta, depending on scanner manufacturer.



A 4 chamber view of the heart using SSFP cine imaging. Compare the image orientation (4 chamber) with the short axis view of the movie above

Infarct imaging using contrast

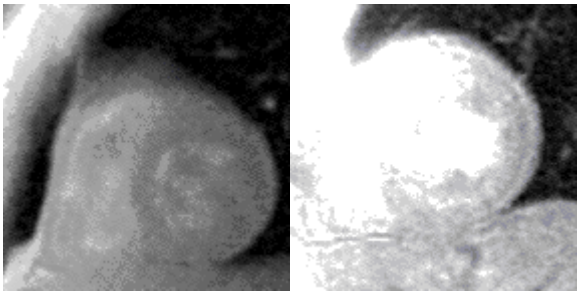
Scar is best seen after giving a contrast agent, typically one containing gadolinium bound to DTPA. With a special sequence, Inversion Recovery (IR) normal heart muscle appears dark, whilst areas of infarction appear bright white.



CMR in the 4 chamber view comparing the cine (left) with the late gadolinium image using inversion recovery (right). The subendocardial infarct is clearly seen. Fat around the heart also appears white.

Perfusion

In angina, the heart muscle is starved of oxygen by a coronary artery narrowing, especially during stress. This appears as a transient perfusion defect when a dose of contrast is given into a vein. Knowing whether a perfusion defect is present and where it is helps guide intervention and treatment for coronary artery narrowings.



CMR perfusion. Contrast appears in the right ventricle then left ventricle before blushing into the muscle, which is normal (left) and abnormal (right, an inferior perfusion defect).

Uses

In the investigation of cardiovascular disease the physician has a wide variety of tools available. The key disadvantages of CMR are limited availability, expense, operator dependence and a lack of outcome data. The key advantages are image quality, non-invasiveness, accuracy, versatility and no ionising radiation.

A good overview of the clinical indications for CMR can be found here and here

Children and congenital heart disease

Congenital heart defects are the most common type of major birth defect. Accurate diagnosis is essential for the development of appropriate treatment plans. CMR can provide comprehensive information about the nature of congenital hearts defects in a safe fashion without using x-rays or entering the body. It is rarely used as the first or sole diagnostic test for congenital heart disease. Rather, it is typically used in concert with other diagnostic techniques. In general, the clinical reasons for a CMR examination fall into one or more of the following categories: 1) when echocardiography (cardiac ultrasound) cannot provide sufficient diagnostic information, 2) as an alternative to diagnostic cardiac catheterization which involve risks including x-ray radiation exposure, 3) to obtain diagnostic information for which CMR offers unique advantages such as blood flow measurement or identification of cardiac masses, and 4) when clinical assessment and other diagnostic tests are inconsistent. Examples of conditions in which CMR is often used include tetralogy of Fallot, transposition of the great arteries, coarctation of the aorta, single ventricle heart disease, abnormalities of the pulmonary veins, atrial septal defect, connective tissue diseases such as Marfan syndrome, vascular rings, abnormal origins of the coronary arteries, and cardiac tumors.

CMR examinations in children typically last 15 to 60 minutes. In order to avoid blurry images the child must remain very still during the examination. In general, most children 7 years of age and older can cooperate sufficiently for a good quality examination. Providing an age-appropriate explanation of the procedure to the child in advance will increase the likelihood of a successful study. After proper safety screening, parents can be allowed into the MRI scanner room to help their child complete the examination. Some centers will allow children to listen to music or watch movies through a specialized MRI-compatible audiovisual system to reduce anxiety and improve cooperation. If the child cannot cooperate sufficiently, sedation with intravenous medications or general anesthesia may be necessary. In very young babies, it may be possible to perform the examination while they are in a natural sleep.

Different magnet types

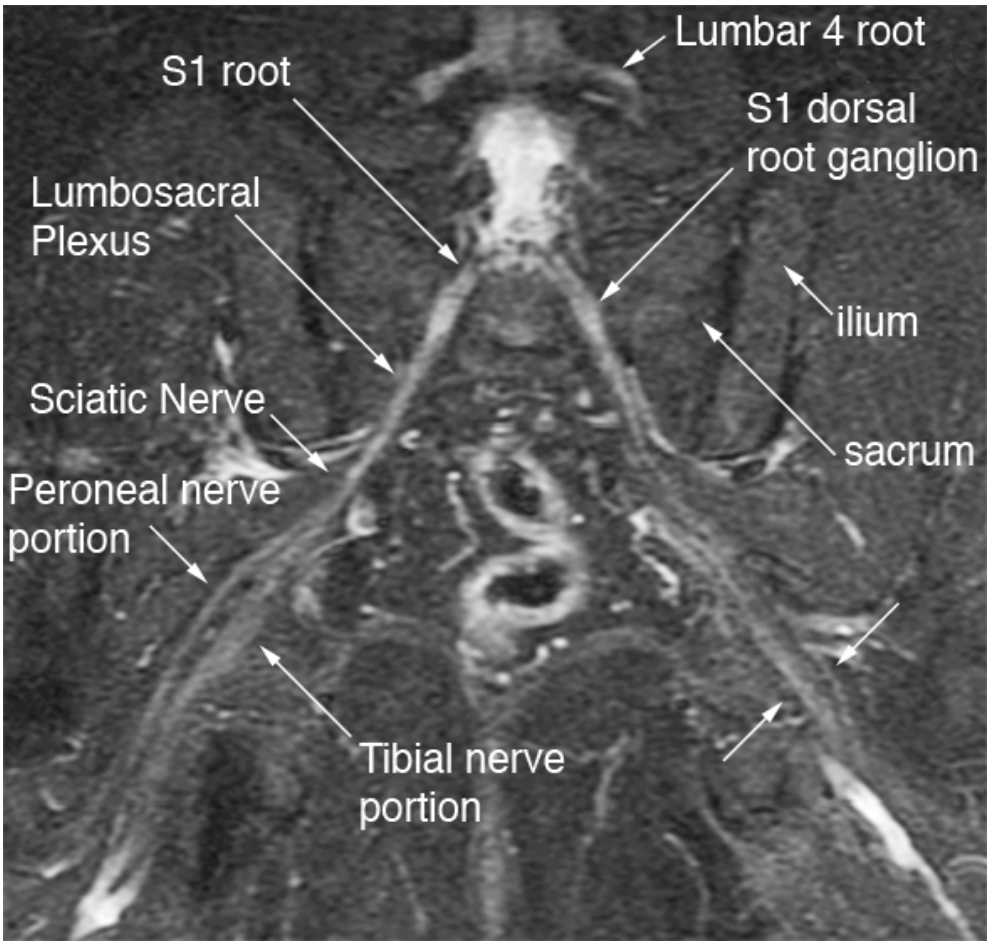
CMR scanners have to be modern. 'Open' magnet are not so good for cardiac as they do not cope with the beating heart very well. There are two magnet strengths mainly in use in CMR - 1.5 Tesla and 3 Tesla. The 3 Tesla has advantages as it potentially doubles the amount of information acquired in the same. It offers particular advantages for perfusion. The downside of 3Tesla is cost and potentially artefact degrading the pictures.

Training

Training is being increasingly protocolised and is now formal with stages of training and accreditation. A resource for anyone thinking about CMR as a career can be found here

Chapter 14

Magnetic Resonance Neurography



Bilateral Split Sciatic Nerve

Magnetic resonance neurography (MRN) is the direct imaging of nerves in the body using special modifications of magnetic resonance imaging. The technique obtains a true detailed image of a nerve in which the resonance signal arises from in the nerve itself

rather than from surrounding tissues or from fat in the nerve lining. Because of the intraneural source of the image signal, the image provides a medically useful set of information about the internal state of the nerve such as the presence of irritation, nerve swelling (edema), compression, pinch or injury. Standard MR images can show the outline of some nerves in portions of their courses but does not show the intrinsic signal from nerve water. MR Neurography is used to evaluate major nerve compressions such as those affecting the sciatic nerve (e.g. piriformis syndrome), the brachial plexus nerves (e.g. thoracic outlet syndrome), the pudendal nerve, or virtually any named nerve in the body. A related technique for imaging neural tracts in the brain and spinal cord is called magnetic resonance tractography or diffusion tensor imaging.

History and physical basis

Magnetic resonance imaging (MRI) is based on differences in the physical properties of protons in water molecules in different tissues in the body. The protons and the water molecules of which they are part have subtly different movement characteristics that relate to their biophysical surroundings. Because of this, MRI is capable of differentiating one tissue from another; this provides "tissue contrast." From the time of the first clinical use of MRI in the mid 1970s until 1992, however, despite the active work of many thousands of researchers, there was no reliable method for visualizing nerve. In some parts of the body, nerves could be observed as areas of absent signal delineated by bright fat, or as bland grey structures that could not be reliably distinguished from other similar-appearing structures in cross sectional images.

In 1992, Aaron Filler and Franklyn Howe, working at St. George's Hospital Medical School in London, succeeded in identifying the unique water properties of nerve water that would make it possible to generate tissue-specific nerve images. The result was an initial "pure" nerve image in which every other tissue was made to disappear leaving behind only the image of the nerves. The initial pure nerve image served as a "Rosetta Stone" leading to discovery of a series of other MRI pulse sequence techniques that would make nerves imageable as well. All of these methods are applicable for any nerve anywhere in the body. Further, because they demonstrate water signal arising in the neural tissue itself, they can also reveal abnormalities that affect only the nerve and that do not affect surrounding tissues. More than three million patients seek medical attention every year for nerve-related disorders such as sciatica, carpal tunnel syndrome or various other nerve injuries, yet before 1992, no radiologists were trained to image nerves, and most physicians believed it simply could not be done usefully

There are two main physical bases for the imaging discovery. Firstly, it was known at the time that water diffused preferentially along the long axis of neural tissue in the brain – a property called "anisotropic diffusion". Diffusion MRI had been developed to take advantage of this phenomenon to show contrast between white matter and grey matter in the brain. However, diffusion MRI proved ineffective for imaging of peripheral nerves for reasons that were not initially clear. Filler and Howe discovered that the problem was that the most of the image signal in nerve came from protons that were not involved in anisotropic diffusion. They developed a collection of methods to suppress the "isotropic

signal" and this resulted in allowing the anisotropic signal to be unmasked. This was based on the discovery that Chemical Shift Selection could be used to suppress "short T2 water" in the nerve and that this mostly affected isotropic water.

The endoneurial fluid compartment in nerve can be unmasked by similar techniques resulting in a "T2" based neurography as well as the original diffusion based neurography technique. Endoneurial fluid increases when nerve is compressed, irritated or injured, leading to nerve image hyperintensity in an MR Neurography image. Subsequent research has further demonstrated the biophysical basis for the ability of MR Neurography to show nerve injury and irritation.

Measurements of the T2 relaxation rate of nerve by Filler and Howe revealed that previous reports of a short relaxation time were wrong and that—once signal from lipid protons was suppressed—the primary image signal from nerve had long T2 relaxation rates best imaged with pulse sequence echo times in the range of 50 to 100 milliseconds. In addition, they later showed that T2-neurography differs from most other MR imaging in that the conspicuity or relative prominence of nerve is affected by the angle of voxel orientation during the acquisition of the image. When acquisitions are done with echo times below 40 milliseconds, there can be "magic angle effects" that provide some spurious information, so MR Neurography is always done with echo times greater than 40 milliseconds. The need for long echo times also characterizes the type of inversion recovery fat suppression sequences used for neurography nerve imaging.

Within a few months of the initial findings on diffusion-based peripheral nerve imaging, the diffusion technique for peripheral nerve imaging was adapted to permit for visualization of neural tracts in the spinal cord and brain via Diffusion Tensor Imaging.

Clinical uses

The most significant impact of MR Neurography is on the evaluation of the large proximal nerve elements such as the brachial plexus (the nerves between the cervical spine and the underarm that innervate shoulder, arm and hand), the lumbosacral plexus (nerves between the lumbosacral spine and legs), the sciatic nerve in the pelvis, as well as other nerves such as the pudendal nerve that follow deep or complex courses.

Neurography has also been helpful for improving image diagnosis in spine disorders. It can help identify which spinal nerve is actually irritated as a supplement to routine spinal MRI. Standard spinal MRI only demonstrates the anatomy and numerous disk bulges, bone spurs or stenoses that may or may not actually cause nerve impingement symptoms.

Many nerves, such as the median and ulnar nerve in the arm or the tibial nerve in the tarsal tunnel, are just below the skin surface and can be tested for pathology with electromyography, but this technique has always been difficult to apply for deep proximal nerves. MR Neurography has greatly expanded the efficacy of nerve diagnosis by allowing uniform evaluation of virtually any nerve in the body.

There are numerous reports dealing with specialized uses of MR Neurography for nerve pathology such as cervical radiculopathy, guidance for nerve blocks, demonstration of cysts in nerves, carpal tunnel syndrome, and obstetrical brachial plexus palsy. In addition several formal large scale outcome trials carried out with high quality "Class A" methodology have been published that have verified the clinical efficacy and validity of MR Neurography.

Reliance on MR Neurography has become widespread in neurology and neurosurgery as the implications of its value in diagnosing various causes of sciatica has become clear. There are 1.5 million lumbar MRI scans performed in the US each year for sciatica, leading to surgery for a herniated disk in about 300,000 patients per year. Of these, about 100,000 surgeries fail. Therefore there is successful treatment for sciatica in just 200,000 and failure of diagnosis or treatment in up to 1.3 million annually in the US alone. The success rate of the paradigm of lumbar MRI and disk resection for treatment of sciatica is therefore about 15%(Filler 2005). Neurography has been applied increasingly to evaluate the distal nerve roots, lumbo-sacral plexus and proximal sciatic nerve in the pelvis and thigh to find other causes of sciatica. It is increasingly important for brachial plexus imaging and for the diagnosis of thoracic outlet syndrome. Active research and development in the clinical use of diagnostic neurography has taken place at Johns Hopkins, the Mayo Clinic, UCLA, UCSF, Harvard, the University of Washington in Seattle, University of London, and Oxford University as well as through the Neurography Institute. Courses have been offered for radiologists on an annual basis at the annual meetings of the Radiological Society of North America (RSNA), and at the International Society for Magnetic Resonance in Medicine and for surgeons at the annual meetings of the American Association of Neurological Surgeons and the Congress of Neurological Surgeons. The use of imaging for diagnosis of nerve disorders represents a change from the way most physicians were trained to practice over the past several decades, but it is increasingly becoming a standard of care when older routine tests fail to identify the diagnosis for nerve related disorders. The New England Journal of Medicine in July 2009 published a report on whole body neurography using a diffusion based neurography technique. This signals appreciation by the editors of the leading medical journal that MR Neurography is now of interest to all physicians. In 2010, RadioGraphics - a publication of the Radiological Society of North America that serves to provide continuing medical education to radiologists - published an article series taking the position that Neurography has an important role in the evaluation of entrapment neuropathies.

MR Neurography does not pose any diagnostic disadvantage relative to standard MR because Neurography studies typically include high resolution standard MRI image series for anatomical reference along with the neurographic sequences. However, the patient will generally have a longer time in the scanner compared to a routine MRI scan. MR Neurography is very demanding of the imaging system so it can only be performed in 1.5 tesla cylindrical type scanners and can't really be done effectively in lower power "open" MR scanners - this can pose significant challenges for claustrophobic patients. Although it has been in use for fifteen years and is the subject of more than 150 research publications, some insurance companies still classify this test as experimental and decline reimbursement. There is no documented standard by which insurance companies are

required to advance a technique from "experimental" to "indicated" so patients may need to file appeals with their insurance company to try to recoup out of pocket costs.

Chapter 15

Magnetoencephalography

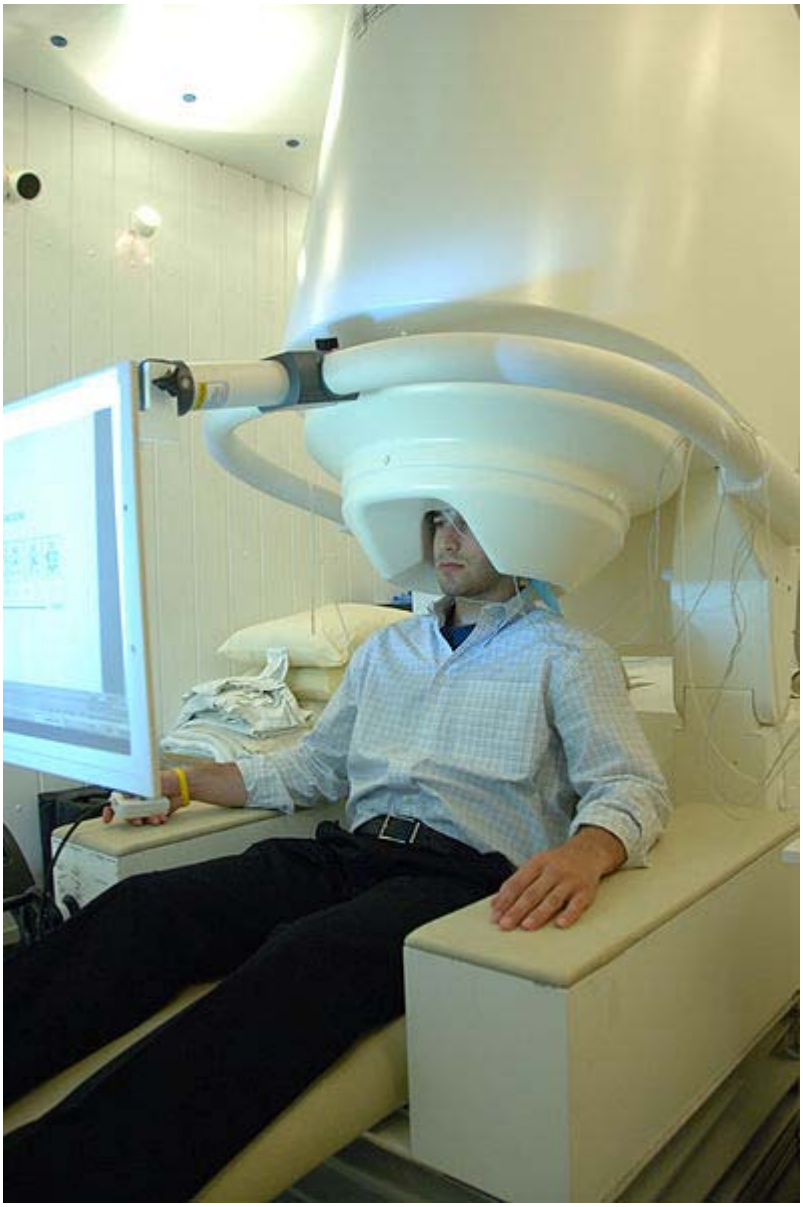
Magnetoencephalography (**MEG**) is a technique for mapping brain activity by recording magnetic fields produced by electrical currents occurring naturally in the brain, using arrays of SQUIDs (superconducting quantum interference devices). Applications of MEG include basic research into perceptual and cognitive brain processes, localizing regions affected by pathology before surgical removal, determining the function of various parts of the brain, and neurofeedback.

History of MEG

MEG signals were first measured by University of Illinois physicist David Cohen in 1968, before the availability of the SQUID, using a copper induction coil as the detector. To reduce the magnetic background noise, the measurements were made in a magnetically shielded room. The coil detector was barely sensitive enough, resulting in poor, noisy MEG measurements that were difficult to use. Later, Cohen built a better shielded room at MIT, and used one of the first SQUID detectors, just developed by James E. Zimmerman, a researcher at Ford Motor Company, to again measure MEG signals. This time the signals were almost as clear as those of EEG. This stimulated the interest of physicists who had been looking for uses of SQUIDs. Subsequently, various types of spontaneous and evoked MEGs began to be measured.

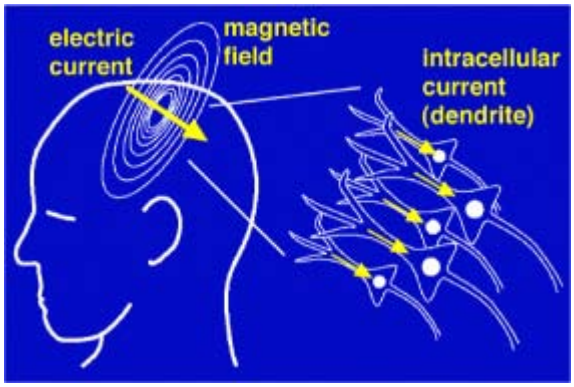
At first, a single SQUID detector was used to successively measure the magnetic field at a number of points around the subject's head. This was cumbersome, and in the 1980s, MEG manufacturers began to arrange multiple sensors into arrays to cover a larger area of the head. Present-day MEG arrays are set in helmet-shaped dewar that typically contain 300 sensors, covering most of the head. In this way, MEGs of a subject or patient can now be accumulated rapidly and efficiently.

The basis of the MEG signal



Patient undergoing an MEG

Synchronized neuronal currents induce weak magnetic fields. At 10 femtotesla (fT) for cortical activity and 10^3 fT for the human alpha rhythm, the brain's magnetic field is considerably smaller than the ambient magnetic noise in an urban environment, which is on the order of 10^8 fT or 0.1 μT. The essential problem of biomagnetism is thus the weakness of the signal relative to the sensitivity of the detectors, and to the competing environmental noise.



Origin of the brain's magnetic field. The electric current also produces the EEG signal.

The MEG (and EEG) signals derive from the net effect of ionic currents flowing in the dendrites of neurons during synaptic transmission. In accordance with Maxwell's equations, any electrical current will produce an orthogonally oriented magnetic field. It is this field which is measured. The net currents can be thought of as electric dipoles, i.e. currents with a position, orientation, and magnitude, but no spatial extent. According to the right-hand rule, a current dipole gives rise to a magnetic field that flows around the axis of its vector component.

To generate a signal that is detectable, approximately 50,000 active neurons are needed. Since current dipoles must have similar orientations to generate magnetic fields that reinforce each other, it is often the layer of pyramidal cells, which are situated perpendicular to the cortical surface, that give rise to measurable magnetic fields. Bundles of these neurons that are orientated tangentially to the scalp surface project measurable portions of their magnetic fields outside of the head, and these bundles are typically located in the sulci. Researchers are experimenting with various signal processing methods in the search for methods that detect deep brain (i.e., non-cortical) signal, but no clinically useful method is currently available.

It is worth noting that action potentials do not usually produce an observable field, mainly because the currents associated with action potentials flow in opposite directions and the magnetic fields cancel out. However, action fields have been measured from peripheral nerves.

Magnetic shielding

Since the magnetic signals emitted by the brain are on the order of a few femtoteslas, shielding from external magnetic signals, including the Earth's magnetic field, is necessary. Appropriate magnetic shielding can be obtained by constructing rooms made of aluminium and mu-metal for reducing high-frequency and low-frequency noise, respectively.

Entrance to MSR, showing the separate shielding layers

Magnetically shielded room (MSR)

A magnetically shielded room (MSR) model consists of three nested main layers. Each of these layers is made of a pure aluminium layer, plus a high permeability ferromagnetic layer, similar in composition to molybdenum permalloy. The ferromagnetic layer is supplied as 1 mm sheets, while the innermost layer is composed of four sheets in close contact, and the outer two layers are composed of three sheets each. Magnetic continuity is maintained by overlay strips. Insulating washers are used in the screw assemblies to ensure that each main layer is electrically isolated. This helps eliminate radio frequency radiation, which would degrade SQUID performance. Electrical continuity of the aluminium is also maintained by aluminium overlay strips to ensure AC eddy-current shielding, which is important at frequencies greater than 1 Hz. The junctions of the inner layer are often electroplated with silver or gold to improve conductivity of the aluminium layers.

Active shielding system

Active systems are designed for three dimensional noise cancellation. To implement an active system, low-noise fluxgate magnetometers are mounted at the center of each surface and oriented orthogonally to it. This negatively feeds a DC amplifier through a low-pass network with a slow falloff to minimize positive feedback and oscillation. Built into the system are shaking and degaussing wires. Shaking wires increase the magnetic permeability, while the permanent degaussing wires are applied to all surfaces of the inner main layer to degauss the surfaces. Moreover, noise cancellation algorithms can reduce both low-frequency and high-frequency noise. Modern systems have a noise floor of around 2–3 $fT/Hz^{0.5}$ above 1 Hz.

Source localization

The inverse problem

The challenge posed by MEG is to determine the location of electric activity within the brain from the induced magnetic fields outside the head. Problems such as this, where model parameters (the location of the activity) have to be estimated from measured data (the SQUID signals) are referred to as *inverse problems* (in contrast to *forward problems* where the model parameters (e.g. source location) are known and the data (e.g. the field at a given distance) is to be estimated.) The primary difficulty is that the inverse problem does not have a unique solution (i.e., there are infinite possible "correct" answers), and the problem of defining the "best" solution is itself the subject of intensive research. Possible solutions can be derived using models involving prior knowledge of brain activity.

The source models can be either over-determined or under-determined. An over-determined model may consist of a few point-like sources ("equivalent dipoles"), whose locations are then estimated from the data. Under-determined models may be used in cases where many different distributed areas are activated ("distributed source solutions"): there are infinitely many possible current distributions explaining the measurement results, but the most likely is selected. Localization algorithms make use of given source and head models to find a likely location for an underlying focal field generator.

Localization algorithms using overdetermined models operate by expectation-maximization: the system is initialized with a first guess. A loop is started, in which a forward model is used to simulate the magnetic field that would result from the current guess. The guess is adjusted to reduce the discrepancy between the simulated field and the measured field. This process is iterated until convergence.

The extent to which the constraint-free MEG inverse problem is ill-posed cannot be overemphasized. If one's goal is to estimate the current density within the human brain with say a 5mm resolution then it is well established that the vast majority of the information needed to perform a unique inversion must come not from the magnetic field measurement but rather from the constraints applied to the problem. Furthermore, even when a unique inversion is possible in the presence of such constraints said inversion can be unstable.

Magnetic source imaging

The estimated source locations can be combined with magnetic resonance imaging (MRI) images to create magnetic source images (MSI). The two sets of data are combined by measuring the location of a common set of fiducial points marked during MRI with lipid markers and marked during MEG with electrified coils of wire that give off magnetic fields. The locations of the fiducial points in each data set are then used to define a

common coordinate system so that superimposing the functional MEG data onto the structural MRI data ("coregistration") is possible.

A criticism of the use of this technique in clinical practice is that it produces colored areas with definite boundaries superimposed upon an MRI scan: the untrained viewer may not realize that the colors do not represent a physiological certainty, because of the relatively low spatial resolution of MEG, but rather a probability cloud derived from statistical processes. However, when the magnetic source image corroborates other data, it can be of clinical utility.

Dipole model source localization

A widely accepted source-modeling technique for MEG involves calculating a set of equivalent current dipoles (ECDs), which assumes the underlying neuronal sources to be focal. This dipole fitting procedure is non-linear and over-determined, since the number of unknown dipole parameters is smaller than the number of MEG measurements. Automated multiple dipole model algorithms such as MUSIC (MUltiple SIgnal Classification) and MSST (MultiStart Spatial and Temporal) modeling are applied to the analysis of MEG responses. The limitations of dipole models for characterizing neuronal responses are (1) difficulties in localizing extended sources with ECDs, (2) problems with accurately estimating the total number of dipoles in advance, and (3) dependency on dipole location, especially depth in the brain.

Distributed Source Models

Unlike multiple-dipole modeling, distributed source models divide the source space into a grid containing a large number of dipoles. The inverse problem is to obtain the dipole moments for the grid nodes. As the number of unknown dipole moments is much greater than the number of MEG sensors, the inverse solution is highly underdetermined, so additional constraints are needed to reduce ambiguity of the solution. The primary advantage of this approach is that no prior specification of the source model is necessary. However, the resulting distributions may be difficult to interpret, because they only reflect a "blurred" (or even distorted) image of the true neuronal source distribution. The matter is complicated by the fact that spatial resolution depends strongly on several parameters such as brain area, depth, orientation, number of sensors etc.

Independent component analysis (ICA)

Independent component analysis (ICA) is another signal processing solution that separates different signals that are statistically independent in time. It is primarily used to remove artifacts such as blinking, eye muscle movement, facial muscle artifacts, cardiac artifacts, etc. from MEG and EEG signals that may be contaminated with outside noise. However, ICA has poor resolution of highly correlated brain sources.

MEG use in the field

In research, MEG's primary use is the measurement of time courses of activity. MEG can resolve events with a precision of 10 milliseconds or faster, while functional MRI (fMRI), which depends on changes in blood flow, can at best resolve events with a precision of several hundred milliseconds. MEG also accurately pinpoints sources in primary auditory, somatosensory and motor areas. For creating functional maps of human cortex during more complex cognitive tasks, MEG is most often combined with fMRI, as the methods complement each other. Neuronal (MEG) and hemodynamic (fMRI) data do not necessarily agree, in spite of the tight relationship between local field potentials (LFP) and blood oxygenation level dependent (BOLD) signals. MEG and BOLD signals may originate from the same source (though the BOLD signals are filtered through the hemodynamic response).

Recent studies have reported successful classification of patients with multiple sclerosis, Alzheimer's disease, schizophrenia, Sjögren's syndrome, chronic alcoholism, and facial pain. MEG can be used to distinguish these patients from healthy control subjects, suggesting a future role of MEG in diagnostics.

Focal epilepsy

The clinical uses of MEG are in detecting and localizing pathological activity in patients with epilepsy, and in localizing eloquent cortex for surgical planning in patients with brain tumors or intractable epilepsy. The goal of epilepsy surgery is to remove the epileptogenic tissue while sparing healthy brain areas. Knowing the exact position of essential brain regions (such as the primary motor cortex and primary sensory cortex, visual cortex, and areas involved in speech production and comprehension) helps to avoid surgically induced neurological deficits. Direct cortical stimulation and somatosensory evoked potentials recorded on ECoG are considered the gold standard for localizing essential brain regions. These procedures can be performed either intraoperatively or from chronically indwelling subdural grid electrodes. Both are invasive.

Noninvasive MEG localizations of the central sulcus obtained from somatosensory evoked magnetic fields show strong agreement with these invasive recordings. MEG studies assist in clarification of the functional organization of primary somatosensory cortex and to delineate the spatial extent of hand somatosensory cortex by stimulation of the individual digits. This agreement between invasive localization of cortical tissue and MEG recordings shows the effectiveness of MEG analysis and indicates that MEG may substitute invasive procedures in the future.

Fetal MEG

MEG has been used to study cognitive processes such as vision, audition and language processing in fetuses and newborns.

Comparison with related techniques

MEG has been in development since the 1960s but has been greatly aided by recent advances in computing algorithms and hardware, and promises improved spatial resolution coupled with extremely high temporal resolution (better than 1 ms). Since the MEG signal is a direct measure of neuronal activity, its temporal resolution is comparable with that of intracranial electrodes.

MEG complements other brain activity measurement techniques such as electroencephalography (EEG), positron emission tomography (PET), and fMRI. Its strengths consist in independence of head geometry compared to EEG (unless ferromagnetic implants are present) and non-invasiveness, as opposed to PET.

MEG vs. EEG

Although EEG and MEG signals originate from the same neurophysiological processes, there are important differences. Magnetic fields are less distorted than electric fields by the skull and scalp, which results in a better spatial resolution of the MEG. Whereas scalp EEG is sensitive to both tangential and radial components of a current source in a spherical volume conductor, MEG detects only its tangential components. MEG therefore measures activity in the sulci selectively, whereas scalp EEG measures activity both in the sulci and at the top of the cortical gyri. EEG is therefore sensitive to activity in more brain areas, but activity that is visible in MEG can also be localized with more accuracy.

Scalp EEG is sensitive to extracellular volume currents produced by postsynaptic potentials. MEG primarily detects intracellular currents associated with these synaptic potentials because the field components generated by volume currents tend to cancel out in a spherical volume conductor The decay of magnetic fields as a function of distance is more pronounced than for electric fields. MEG is therefore more sensitive to superficial cortical activity, which makes it useful for the study of neocortical epilepsy. Finally, MEG is reference-free, while scalp EEG relies on a reference that, when active, makes interpretation of the data difficult.

Chapter 16

Medical Radiography

Radiography is the use of ionizing electromagnetic radiation such as X-rays to view objects. Although not technically radiographic techniques, imaging modalities such as PET and MRI are sometimes grouped in radiography because the radiology department of hospitals handle all forms of imaging. Treatment using radiation is known as radiotherapy.

History

Radiography started in 1895 with the discovery of X-rays (later also called Röntgen rays after the man who first described their properties in rigorous detail), a type of electromagnetic radiation. Soon these found various applications, from helping to find shoes that fit, to the more lasting medical uses. X-rays were put to diagnostic use very early, before the dangers of ionising radiation were discovered. Initially, many groups of staff conducted radiography in hospitals, including physicists, photographers, doctors, nurses, and engineers. The medical speciality of radiology grew up around the new technology, and this lasted many years. When new diagnostic tests involving X-rays were developed, it was natural for the radiographers to be trained and adopt this new technology. This happened first with fluoroscopy, computed tomography (1960s), and mammography. Ultrasound (1970s) and magnetic resonance imaging (1980s) was added to the list of skills used by radiographers because they are also medical imaging, but these disciplines do not use ionising radiation or X-rays. Although a nonspecialist dictionary might define radiography quite narrowly as "taking X-ray images", this has only been part of the work of an "X-ray department", radiographers, and radiologists for a very long time. X-rays are also exploited by industrial radiographers in the field of nondestructive testing, where the newer technology of ultrasound is also used.

Diagnostic radiography

Diagnostic radiography involves the use of both ionising radiation and non-ionising radiation to create images for medical diagnoses. The predominant test is still the X-ray (the word X-ray is often used for both the test and the actual film or digital image). X-

rays are the second most commonly used medical tests, after laboratory tests. This application is known as diagnostic radiography. Since the body is made up of various substances with differing densities, X-rays can be used to reveal the internal structure of the body on film by highlighting these differences using attenuation, or the *absorption* of X-ray photons by the denser substances (like calcium-rich bones). Medical diagnostic radiography is undertaken by a specially trained professional called a diagnostic radiographer in the UK, or a radiologic technologist in the USA.

There are several sub-specialities:

Projection radiography

The creation of images by exposing an object to X-rays or other high-energy forms of electromagnetic radiation and capturing the resulting remnant beam (or "shadow") as a latent image is known as "projection radiography." The "shadow" may be converted to light using a fluorescent screen, which is then captured on photographic film, it may be captured by a phosphor screen to be "read" later by a laser (CR), or it may directly activate a matrix of solid-state detectors (DR—similar to a very large version of a CCD in a digital camera). Bone and some organs (such as lungs) especially lend themselves to projection radiography. It is a relatively low-cost investigation with a high diagnostic yield.

Projection radiography uses X-rays in different amounts and strengths depending on what body part is being imaged:

- Hard tissues such as bone require a relatively high energy photon source, and typically a tungsten anode is used with a high voltage (50-150 kVp) on a 3-phase or high-frequency machine to generate braking radiation. Bony tissue and metals are denser than the surrounding tissue, and thus by absorbing more of the X-ray photons they prevent the film from getting exposed as much. Wherever dense tissue absorbs or stops the X-rays, the resulting X-ray film is unexposed, and appears translucent blue, whereas the black parts of the film represent lower-density tissues such as fat, skin, and internal organs, which could not stop the X-rays. This is usually used to see bony fractures, foreign objects (such as ingested coins), and used for finding bony pathology such as osteoarthritis, infection (osteomyelitis), cancer (osteosarcoma), as well as growth studies (leg length, achondroplasia, scoliosis, etc.).

- Soft tissues are seen with the same machine as for hard tissues, but a "softer" or less-penetrating X-ray beam is used. Tissues commonly imaged include the lungs and heart shadow in a chest X-ray, the air pattern of the bowel in abdominal X-rays, the soft tissues of the neck, the orbits by a skull X-ray before an MRI to check for radiopaque foreign bodies (especially metal), and of course the soft tissue shadows in X-rays of bony injuries are looked at by the radiologist for signs of hidden trauma (for example, the famous "fat pad" sign on a fractured elbow).

- Dental radiography uses a small radiation dose with high penetration to view teeth, which are relatively dense. A dentist may examine a painful tooth and gum using X-ray equipment. The machines used are typically single-phase pulsating DC, the oldest and simplest sort. Dental technicians or the dentist may run these machines—radiologic technologists are not required by law to be present.

- Mammography is an X-ray examination of breasts and other soft tissues. This has been used mostly on women to screen for breast cancer, but is also used to view male breasts, and used in conjunction with a radiologist or a surgeon to localise suspicious tissues before a biopsy or a lumpectomy. Breast implants designed to enlarge the breasts reduce the viewing ability of mammography, and require more time for imaging as more views need to be taken. This is because the material used in the implant is very dense compared to breast tissue, and looks white (clear) on the film. The radiation used for mammography tends to be softer (has a lower photon energy) than that used for the harder tissues. Often a tube with a molybdenum anode is used with about 30 000 volts (30 kV), giving a range of X-ray energies of about 15-30 keV. Many of these photons are "characteristic radiation" of a specific energy determined by the atomic structure of the target material (Mo-K radiation).

Other modalities are used in radiography when traditional projection X-ray cannot image what doctors want to see. Below are other modalities included within radiography; they are only summaries and more specific information can be viewed by going to their individual pages:

Fluoroscopy (angiography, gastro-intestinal fluroscopy)

Fluoroscopy is a term invented by Thomas Edison during his early X-ray studies. The name refers to the fluorescence he saw while looking at a glowing plate bombarded with X-rays.

This is a technique that provides moving projection radiographs of lower quality. Fluoroscopy is mainly performed to view movement (of tissue or a contrast agent), or to guide a medical intervention, such as angioplasty, pacemaker insertion, or joint repair/replacement. The latter are often carried out in the operating theatre, using a portable fluoroscopy machine called a C-arm. It can move around the surgery table and make digital images for the surgeon.

Angiography is the use of fluoroscopy to view the cardiovascular system. An iodine-based contrast is injected into the bloodstream and watched as it travels around. Since liquid blood and the vessels are not very dense, a contrast with high density (like the large iodine atoms) is used to view the vessels under X-ray. Angiography is used to find aneurysms, leaks, blockages (thromboses), new vessel growth, and placement of catheters and stents. Balloon angioplasty is often done with angiography.

Fluoroscopy can be used to examine the digestive system using a substance which is opaque to X-rays, (usually barium sulfate or gastrografin), which is introduced into the digestive system either by swallowing or as an enema. This is normally as part of a *double contrast technique,* using positive and negative contrast. Barium sulfate coats the walls of the digestive tract (positive contrast), which allows the shape of the digestive tract to be outlined as white or clear on an X-ray. Air may then be introduced (negative contrast), which looks black on the film. The barium meal is an example of a contrast agent swallowed to examine the upper digestive tract. Note that while soluble barium compounds are very toxic, the insoluble barium sulfate is non-toxic because its low solubility prevents the body from absorbing it.

- A number of substances have been used as positive contrast agents: silver, bismuth, caesium, thorium, tin, zirconium, tantalum, tungsten and lanthanide compounds have been used as contrast agents. The use of thoria (thorium dioxide) as an agent was rapidly stopped as thorium causes liver cancer.

Most modern injected radiographic positive contrast media are iodine-based. Patients who suffer from allergy to shellfish may be allergic to iodine, and should consult their physician regarding pre-medication to lessen risk of allergic reaction. Iodinated contrast comes in two forms: ionic and non-ionic compounds. Non-ionic contrast is significantly more expensive than ionic (approximately three to five times the cost), however, non-ionic contrast tends to be safer for the patient, causing fewer allergic reactions and uncomfortable side effects such as hot sensations or flushing. Most imaging centers now use non-ionic contrast exclusively, finding that the benefits to patients outweigh the expense.

- Negative radiographic contrast agents are air and carbon dioxide (CO_2). The latter is easily absorbed by the body and causes less spasm. It can also be injected into the blood, where air absolutely cannot.

Dual energy X-ray absorptiometry

DEXA, or bone densitometry, is used primarily for osteoporosis tests. It is not projection radiography, as the X-rays are emitted in 2 narrow beams that are scanned across the patient, 90 degrees from each other. Usually the hip (head of the femur), lower back (lumbar spine) or heel (calcaneum) are imaged, and the bone density (amount of calcium) is determined and given a number (a T-score). It is not used for bone imaging, as the image quality is not good enough to make an accurate diagnostic image for fractures, inflammation etc. It can also be used to measure total body fat, though this isn't common. The radiation dose received from DEXA scans is very low, much lower than projection radiography examinations.

Computed tomography

Computed tomography or CT scan (previously known as CAT scan, the "A" standing for "axial") uses a high amount of ionizing radiation (in the form of X-rays) in conjunction

with a computer to create images of both soft and hard tissues. These images look as though the patient was sliced like bread (thus, "tomography"-- "tomo" means "slice"). The machine looks similar to an MRI machine to many patients, but is not related. The exams are generally short, most lasting only as long as a breath-hold. Contrast agents are often used, depending on the tissues needing to be seen. Radiographers perform these examinations, sometimes in conjunction with a radiologist (for instance, when a radiologist performs a CT-guided biopsy).

Technical considerations

X-ray photons are formed in events involving electrons and are the mainly form of ionizing electromagnetic radiation used in medical radiography. This radiation is much more energetic than the more familiar types such as radio waves and visible light. Proper production and detection of photons are important in the creation of good radiograms.

Photon production

X-ray radiation for medical imaging is typically produced by X-ray tubes, which operate through bombarding the anode with high energy electrons emitted from a hot cathode. Image sharpness, contrast, and patient dosage are important considerations in medical radiography and these requirements determined the desired energies of the tube, the type of material used on the anode, and the method in which the power is generated to drive the tube. Although the technical definition of x-rays range from 1-700 keV, medical x-rays typically use 5-150 keV x-rays. The photons emitted come in discrete bands of energy corresponding to the material of the anode, and the undesired bands are removed. Choice of the anode and its emitted radiation energies depends on the application and the tissues being imaged, for instance molybdenum is often used in mammography because of its 20 keV x-rays. Too high radiation energies will result in poor pictures since the radiation cannot be readily attenuated, however too low energies will increase the radiation dosage of the patient without improvements in image quality.

Sharpness of a radiographic image is strongly determined by the size of the x-ray source. This is determined by the area of the electron beam hitting the anode. A large photon source results in more blurring in the final image and is worsened by an increase in image formation distance. This blurring can be measured as a contribution to the modulation transfer function of the imaging system.

Power generation

The power used by the x-ray tube is generated by a specialized generator, which supplies the voltage and current required to drive the tube. The generator needs to supply high voltages with small exposure times. An exposure thus can be described by two factors:

1. The *peak voltage* of the cathode to anode
2. The *milliamprere seconds* exposure time

These variables can be controlled by the operator but are more typically assigned automatically by the x-ray machinery through sampling the emitted radiation. Power generators convert standard 120 or 220 volt AC to higher DC voltages and typically employ rectified and filtered multiphase transformers which maintain a constant voltage and can be turn rapidly on and off for millisecond exposures.

Photon detection

Photons images that have been shadowed from an imaging subject must be detected at high fidelity and resolution to allow for diagnosis. There are three main types of image detection methods used namely: film/screens, image intensifiers, and digital detectors, with the latter fast becoming the standard for x-ray image detection. The ability of an x-ray detector to produce high-quality images is determined largely by the modulation transfer function (MTF) and detective quantum efficiency (DQE) of the system.

Film/Screens

X-ray film is almost always used in conjunction with x-ray sensitive screen because high resolution film is quite poor at detecting x-rays. These screens contain rare earth minerals and phosphor materials thatconvert x-ray radiation to visible light or lows EM energies to which the film is sensitive. Screen generally have to have good contrast, dynamic range, and resolution, with the former two factors being competing properties. The resolution of the screen also affects the sensitivity of the detectors since more sensitive screens are generally thicken, which causes the more blurring because of spreading light.

The film speed also play a factor in image quality. Higher speeds are more sensitive to photons but are generally lower in resolution and more susceptible to noise. Lower speed films produce images of good resolution and dynamic range but requires more photons for exposure and increases the radiation dosage of the subject.

Image intensifiers and array detectors

Image intensifiers are analog devices that readily convert the acquired x-ray image into one visible on a video screen. This device is made of a vacuum tube with a wide input surface coated on the inside with caesium iodide (CsI). When hit by x-rays material phosphors which causes the photocathode adjacent to it to emit electrons. These electron are then focus using electron lenses inside the intensifier to an output screen coated with phosphorescent materials. The image from the output can then be recorded via a camera and displayed.

Digital devices known an array detectors are becoming more common in fluoroscopy. These devices are made of discrete pixelated detectors known as TFTs which can either work *indirectly* by using photo detectors that detect light emitted from a scintillator material such as CsI, or *directly* by capturing the electrons produced when the x-rays hit the detector. Direct detector do not tend to experience the blurring or spreading effect

caused by phosphorescent scintillators of or film screens since the detectors are activated directly by x-ray photons.

Obsolete terminology

The term *skiagrapher* was used until about 1918 to mean *radiographer*. It was derived from Ancient Greek words for 'shadow' and 'writer'.