2 Medical imaging methods

The purpose of this chapter is to introduce a classification scheme for medical imaging methods. This is then applied to some established and some novel medical imaging techniques and a set of properties is extracted that characterizes successful imaging methods.

A "medical imaging method" can be defined as a method to image parts of a human or animal, e.g., to acquire data about the tissue, the tissue composition or characteristics, the bones, or even about physiological characteristics using special substances, called tracers, which are injected into the body. The region of interest can be inside the body, i.e., it can be several centimeters below any accessible surface. The scope of this document is limited to such methods, i.e. methods that image only the surface like thermography or only a few mm deep like optical coherence tomography are not discussed.

Established methods for clinical use, which should be discussed for any such scheme of characterization of medical imaging methods, are:

- X-ray imaging
- Computed Tomography (CT)
- UltraSound Imaging (US)
- Magnetic Resonance Imaging (MRI)
- Scintigraphy (Anger camera)
- Single Photon Emission Computed Tomography (SPECT)
- Positron Emission Tomography (PET)

Besides these, other methods, which are less common in clinical use or that are in experimental status, will be considered:

- Electrical Impedance Tomography

B. Gleich, *Principles and Applications of Magnetic Particle Imaging,* Aktuelle Forschung Medizintechnik, DOI 10.1007/978-3-658-01961-7_2, © Springer Fachmedien Wiesbaden 2013

- Diffuse Optical Tomography
- Thermoacoustic/Photoacoustic Imaging
- Electron Paramagnetic Resonance Imaging (EPR)

This thesis will not explain how these methods work in detail, but rather focus on some common features involved in the characterization scheme. These aspects are signal penetration, tissue interaction, and signal confinement.

2.1 Signal penetration

To form an image of an area within a body, it is necessary for the signal to penetrate the tissue. Likewise, it is necessary to acquire the signal that is emitted by the tissue, i.e., information about the tissue. Consequently, it is necessary for any imaging method to use information carriers that penetrate human tissue for at least some centimeters, and preferably more. Table 2.1 lists signals and information carriers that have the ability to penetrate tissue sufficiently. As the inital signal entering the body (send signal) and the signal that carries the information about the tissue (emitted signal) do not need to be of the same type, it is possible to construct candidates for methods of medical imaging by combining one signal type as the send signal with another signal type as the receive signal. This way, one can theoretically construct 21 different medical imaging methods (some are left out, since methods in which *no* signal is emitted from the body do not make a reasonable imaging method—others are not possible for reasons given by the laws of nature).

Low frequency electromagnetic fields (**LF**) are well known from MRI. **X-ray**s are the basis for X-ray imaging and computed tomography (CT), and accoustic waves **elast** are commonly used in ultrasound. Using light **OPT** or atomic particles **ptcl** is currently not common for medical imaging, but the underlying concepts are straightforward. They can be used in the same way as low frequency electromagnetic fields or X-rays.

The information carrier "fluidic matter" (**fluid**) needs some explanation. While the use of fluidic matter as a send signal initially seems

LF:	Low frequency electromagnetic fields (0 Hz to about 1 GHz)
OPT:	Optical / near infrared and red light (1.2 μm to 750 nm)
X-ray:	X-rays, γ-rays (energies above $\approx$10 keV)
elast:	Acoustic waves (0 Hz to $\approx$10 MHz)
ptcl:	Particles at high energies (e.g., electrons, protons, neutrons and neutrinos)
fluid:	Fluidic matter (e.g., something that can be injected using a syringe, e.g a nuclear tracer)
none:	Special case: no signal enters the tissue, but the tissue itself emits signal

Table 2.1: Information carriers used in medical imaging

cryptic, it is actually quite common. One example would be the methods used in nuclear medicine (SPECT, PET), where a radioactive tracer is injected and is "fluidic matter". Another example, which is beyond what could be understand as a "fluid", would be a macroscopic device—to be more specific, it would be possible to acquire an image of a vessel tree by localizing the positions of an RF emitting marker on a catheter. The use of "fluidic matter" as an emitted signal to acquire information about the tissue is theoretically possible, but it is unlikely that it is actually used. A beam of X-rays with a very high intensity, for example, would damage the tissue and a change in the blood composition can be expected. So, theoretically, scanning the patient with the beam bit by bit and drawing and analysing many blood samples, could be used to make an image that would display information about certain tissue characteristics.

The information carrier "Nothing" can only be used in the sense of bringing nothing into the body, as it would, for example, be possible to collect low frequency electrical noise data to map the temperature of deep lying tissue. However, using "Nothing" as an emitted signal would most certainly not result in an image.

It is also possible to use two or more of these information carriers in combination. An example would be the injection of a contrast agent

(e.g., fluid used as a send signal) and imaging with X-ray or MRI (e.g., LF or X-ray used as send and emitted signals).

2.2 Tissue interaction

Another essential feature of an imaging method is the interaction of the information carriers with the tissue[1]. This interaction has to vary with different tissues to generate a tissue specific contrast. Neutrinos, for example, are excellent in penetrating tissue, but the interaction is so low that imaging does not seem to be feasible.

Physics allows for a large number of interactions and it does not seem feasible to describe them all in detail. Nevertheless, the interactions can be classified into two categories:

- an intrinsic interaction with the tissue (without tracer or contrast agent) and
- an interaction with an injected contrast agent or tracer.

An example of the first category would be tissue specific absorption of X-rays, which yields an excellent visualization of bones. An example of the second category would be electron paramagnetic resonance imaging (EPR). The intrinsic concentration of free radicals is very low and an injected tracer generates essentially all the interaction.

For useful medial imaging, the contrast mechanism must be tissue specific. Again, two categories can be observed:

- the tissue specificity is intrinsic (i.e., no further help by tracers or contrast agents is needed)
- the tissue specificity has to be mediated by an injected contrast agent or tracer.

Staying within the example for the first category above, one can observe that bones have a much higher X-ray absorption than the surrounding soft tissue: therefore the excellent visualization of bones. On the other hand, and this constitutes an example for tissue specificity mediated by a tracer or contrast agent, X-ray absorption in blood is very similar to absorption in the vessel walls. Consequently, an X-ray

[1]Tissue in this context also refers to bones and anything else which is present within the body.

absorbing contrast agent is needed to generate a contrast that exposes the vessel lumen.

Taking it all together, the above categories can be combined to form four types of tissue interaction, as listed in Table 2.2.

1 Intrinsic interaction & intrinsic contrast. (e.g., ultrasound, MRI, X-ray, CT)

2 Intrinsic interaction & contrast agent modulates intrinsic interaction (e.g., contrast enhanced MRI)

3 Contrast agent mediated interaction & no tissue contrast agent interaction (e.g., contrast enhanced CT, angiography, hyperpolarized MRI)

4 Contrast agent mediated interaction & agent tissue interaction (e.g., O_2 sensing in EPR, hyperpolarized MRI [2])

Table 2.2: Four types of tissue interaction

Type 1 has the advantage of not needing any contrast agent, which simplifies the examination and workflow. Type 3 essentially images the pure concentration and distribution of a contrast agent, which has the potential to ease image interpretation. Types 2 and 4 have the capability to map tissue parameters.

2.3 Signal confinement/resolution

The third aspect used in characterizing imaging modalities is to look at how they confine the tissue interaction to a small volume. If the interaction is not confined, sufficient spatial resolution and image formation is not possible. There are several ways to confine the interaction[3], the three most important are listed in Table 2.3.

In **i**, at least one of the information carriers has be focused on a small region with a size on the order of the desired resolution. This is possible

[2]Hyperpolarized MRI is an example that is listed in 3 and 4, as it can use different nuclei and different chemical compounds with different imaging sequences.

[3]To form an image, the interaction does not need to be confined directly to the "voxel" of the image. It is also possible to confine the interaction to other geometries and compute the voxels from these resulting signals.

i	geometrical and wave optics (e.g., X-ray, CT, ultrasound)
ii	near field methods (e.g., diffuse optical tomography, electrical impedance tomography)
iii	field-confined interaction (e.g., MRI)

Table 2.3: Methods to confine tissue interaction to small volumes

for X-rays, elastic waves of high enough frequency (e.g., >100 kHz for 1 cm resolution) and some particle rays.

In **ii**, the information carrier cannot be confined. Optical photons, for example, are heavily scattered in most tissues, so that signal propagation is a very diffusive process. Low frequency electromagnetic fields cannot be localized in deep lying tissue by using devices at the surface of the tissue. Still, theoretically, an image with arbitrary resolution can be reconstructed from data obtained at the surface. This can be easily understood in one dimension (cf. Fig. 6.1): The signal from one voxel is convolved with a smooth function. A convolution has an inverse function, as long as the Fourier coefficients do not drop to zero, which is the case for Gauss-like functions, even when very broad. Thus, a high-resolution image can be reconstructed when data are sampled on a fine grid at the surface of the patient. The problem is that the spatial Fourier components of the sampled data containing the high-resolution information rapidly drop to the noise floor. So in practice, resolution hardly reaches 1 cm. [4]

In **iii**, the problems of case **ii** are overcome by confining the interaction using a physical effect that is modulated by a field. This can also be understood as using an interaction with a non-linear response, i.e., doubling all fields in strength does not result in doubling the signal obtained. Exploiting this kind of interaction for spatial confinement was called "zeugmatography" by Lauterbur [Lau73]. The most prominent example is MRI and related techniques. Here, the resonance for a given frequency occurs only for a definite magnetic field. By applying a gradient field, the interaction is confined to a (curved) plane. Another example is the generation of harmonics in ultrasound imaging. As with

[4] Sometimes it is said that this is an *ill posed problem*. This is true, but misleading as e.g., the CT reconstruction is ill posed in the mathematical sense. Still CT images exhibit high resolution.

two-photon techniques in optical microscopy, the non-linear effect of the generation of harmonics strongly increases with the field strength, and therefore confines the interaction to a smaller spot in the focus.

2.4 Overview of existing imaging methods

This section categorizes established imaging methods by their use of information carriers (what type of signals they use), as well as their approach to tissue interaction (how do they generate a contrast) and signal confinement (how do they achieve spatial resolution). Table 2.4 presents the results of the categorization together with the "maturity" of the imaging method (is it already used for routine clinical imaging or is it still in a pre-clinical or even experimental state), which is displayed as a colour code.

One important observation is that there are many methods proposed or used for tomographic imaging in a medical context, but only a few have made it to routine clinical use. Another observation is that methods that utilize ionized, fast particles are rarely used for medical imaging: their use is limited to one method associated with heavy-ion therapy for oncology. The reason for the lack of particle based imaging modalities is probably the potential damage to tissue. Physical effects that involve sufficiently high energy to produce tissue-penetrating particles are also destructive to the tissue. Consequently, using them for general diagnostics is strongly discouraged.

One further observation is that no optical method has reached routine clinical use, although optical methods have good intrinsic tissue contrast and a variety of useful contrast agents exist for use in small animal imaging. Additionally, photoacoustic tomography is an optical method with reasonable resolution. The main problem with optical methods is the low tissue penetration of red and infrared light, which limits their use. The light intensity is reduced to roughly 10% for every cm of tissue. Thus, imaging deeper than 5 cm becomes challenging and at a depth of 10 cm, virtually no photon can penetrate the tissue and return to the surface. Consequently, applications in adult humans are limited mainly to the limbs and the female breast. In the light of such limited potential applications, the economic risks in developing an optical imaging method for clinical use may seem too high.

Furthermore, it is also interesting to notice that no method without

	LF	OPT	X-ray	elast
LF	**MRI (iii,1,2)**[4] *EIT (ii,1)*[3] MIT (ii,1)[1] H-MRI (iii,3,4)[2] O-MRI (iii,4)[2]			*TAT (i,1)*[3] MAT (i,1)[1] MAT-MI (i,1)[1]
OPT		*DOT (ii,1,3,4)*[3] UMOT (i,1,3,4)[2]		PAT (i,1,3,4)[2]
X-ray			**X-ray (i,1,3)**[4] **CT (i,1,3)**[4] **DSA (i,3)**[4] CSCT (i,1)[2]	XAT (i,1,3)[1]
elast	MAET (i,1)[1]	SLI (i,1,3,4)[1]		**US (i,1,3)**[4] **HI (i,1,3)**[4]
ptcl			**ITM (i,1)**[4]	
fluid			**SZG (i,3)**[4] **SPECT (i,3)**[4] **PET (i,3)**[4]	
none	*MTI (ii,1)*[3]	*BLI (ii,1)*[3]		PTT (i,1)[1]

[4]**: Clinically used**
[3]*: Images in human shown*
[2]: In vivo images shown
[1]: In vitro experiments/method proposed

Table 2.4: A selection of established imaging modalities classified by their use of information carriers, their approach to tissue interaction, given arabic numbers as listed in Table 2.2, and signal confinement, given in roman numbers as listed in Table 2.3. The superscripts and the font indicate the maturity of the method. The acronyms used for the imaging methods are listed in Tables 2.5 to 2.7.

a good (type **i** and **iii**) way of confining the tissue interaction to a small volume has reached routine clinical use. A deconvolution of diffusion equations or static Maxwell equations yields resolutions no better than 2 cm in deep tissue. Given such a resolution, only large lesions can be detected, which limits the practical clinical use.

All diagnostic imaging methods used in a clinical context rely on or can be improved by the use of a contrast agent. The use of an injected fluid results in additional contrast with potentially high clinical relevance.

From Table 2.4 it can be observed that elastic waves have a high

MRI: Magnetic Resonance Imaging A strong magnetic field is applied together with a small gradient. A radio-frequency pulse is applied which matches the resonance condition of, e.g., one slice. The "echo" of the resonance is measured while being modulated by the change of gradients. [Lau73]

EIT: Electrical Impedance Tomography The AC electrical impedance between electrodes is measured. [TOK08]

MIT: Magnetic Induction Tomography The magnetic field of eddy currents in tissue is measured. [MHOS04]

DOT: Diffuse Optical Tomography The propagation of light between a collection of points on the tissues surface is measured. [CCL+05]

X-ray: X-ray Projection Imaging The X-ray photons transmitted through the tissue from a point source are displayed. [Rön96]

CT: X-ray Computed Tomography A slice or volume is irradiated with X-rays from many angles and a 2D or 3D image is computed from the transmitted rays. [Hou73]

US: UltraSound Imaging Tissue is irradiated with a focused ultrasound beam and the reflected and scattered ultrasound is measured. [Dus42]

SPECT: Single Photon Emission Computed Tomography A gamma-ray emitter (tracer) is brought into the patient and the emitted photons are collimated and measured. As in CT, the collimated photons are collected from many angles and a 3D image is reconstructed. [KE63]

PET: Positron Emission Tomography A positron emitter (tracer) is brought into the patient. The two annihilation photons are detected in coincidence and the direction of emission is deduced. From the ensemble of these emission directions, a 3D image is computed. [TPPHM75] [CHB73]

PAT: PhotoAcoustic Tomography Red or near infrared light heats the tissue. The tissue expands and thereby emits an acoustic wave. [ZLC+08]

TAT: ThermoAccoustic Tomography A radio wave heats the tissue. The tissue expands and thereby emits an acoustic wave. [KMR+00]

Table 2.5: Abbreviations as used in Table 2.4, together with a a short explanation and references.

potential of interacting with other information carriers. They can be produced by any information carrier by a thermoacoustic effect (even if no known imaging modalities exist).

Although thermoacoustic tomography breast images have been demonstrated with a quality comparable to or even exceeding those

BLI: BioLuminescence Imaging The weak chemo- bio-luminescence of tissue metabolism is measured. [EIJKT90]

SZG: SZintiGraphy The X-ray (gamma-ray) photons from an injected tracer are collimated and detected. [Ang58]

H-MRI: Hyperpolarized MRI Hyperpolarized MRI is like MRI, but the measured magnetization is introduced to the tissue by the injection/inhalation of externally hyperpolarized material. [GKD+08]

O-MRI: Overhauser Overhauser enhanced magnetic resonance works like MRI, but the magnetization of the nuclei is increased by the use of a double-resonance with unpaired electrons. [HMM+08]

DSA: Digital Subtraction Angiography Contrast enhanced X-ray projection imaging, where the image without contrast agent is subtracted. [CSS+80] [OCF+80]

MAT: MagnetoAcoustic Tomography A current is applied to the tissue. In an additional static magnetic field, the current leads to Lorentz forces, which give rise to ultrasound emissions. The ultrasound is detected. [RBW94]

MAT-MI: MagnetoAcoustic Tomography with Magnetic Induction Works like MAT, but the current is not fed to the tissue by electrodes, but by a time-varying magnetic field [YB05].

PTT: Passive Thermoacoustic Tomography The acoustic noise emitted by the tissue is recorded. [PAB00]

ITM: Heavy Ion Therapy Monitoring The distribution of positron emitters produced by heavy ion therapy is imaged using positron emission tomography [PBH08]

Table 2.6: Abbreviations as used in Table 2.4 (continued)

of classical ultrasound imaging, a clinical use does not seem apparent. Possible reasons may be the intrinsic limitations of ultrasound: It does not penetrate the lung and has problems near bones and the (gas filled) intestine. In consequence, a large part of the body is not accessible. An additional problem is that the complex mechanical properties of the tissue (diffraction, scattering, attenuation) significantly limit the practical resolution. Improvements can be expected if the tissue to be imaged is accessible from many angles. Thus practically, thermoacoustic methods are also limited to the limbs and the female breast, which may limit the potential market.

http://www.springer.com/978-3-658-01960-0

Principles and Applications of Magnetic Particle Imaging

Gleich, B.

2014, XII, 118 p. 25 illus., Softcover
ISBN: 978-3-658-01960-0