UNIVERSITY OF TROMSØ UIT

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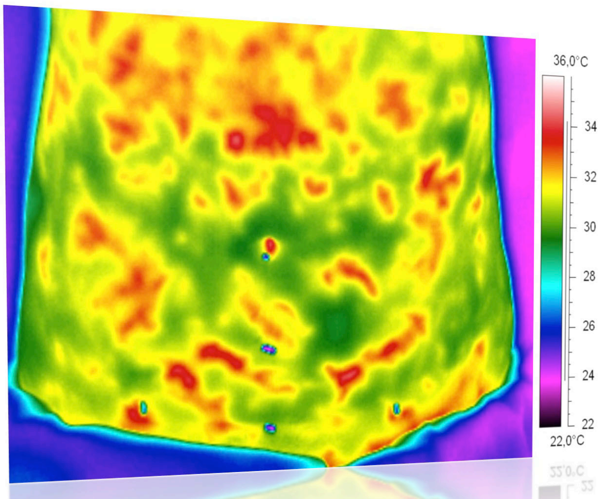
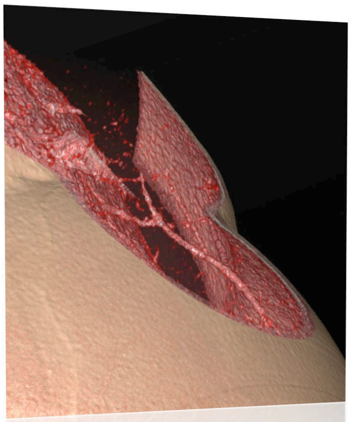
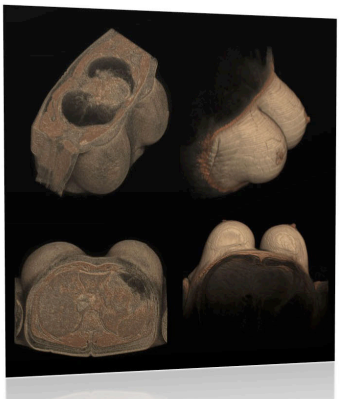
Imaging in plastic surgery

A clinical and experimental study with notes on the history of medical imaging







Sven Weum

A dissertation for the degree of
Philosophiae Doctor

2013

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Friendship is born at that moment when one person says to another:
"What! You too? I thought I was the only one."
C.S. Lewis

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Contents

1. List of papers

Paper I

Åshild Odden Miland, Louis de Weerd, Sven Weum, James B. Mercer

Visualising vascular perfusion in isolated human abdominal skin flaps using dynamic infrared thermography and indocyanine green fluorescence video angiography

European Journal of Plastic Surgery 2008; 31: 235-42

Paper II

Louis de Weerd, Sven Weum, James B. Mercer

The value of dynamic infrared thermography (DIRT) in perforator selection and planning of DIEP flaps

Annals of Plastic Surgery 2009; 63(3): 274-9

Paper III

Sven Weum, James B. Mercer, Louis de Weerd

Perforator mapping in breast reconstruction: A comparative study of dynamic infrared thermography (DIRT), computed tomographic angiography (CTA) and hand-held Doppler

Submitted to Radiology

Paper IV

Sven Weum, Louis de Weerd, Bente Kristiansen

Form stability of Style 410 anatomically shaped cohesive silicone gel-filled breast implant in subglandular breast augmentation evaluated with magnetic resonance imaging

Plastic and Reconstructive Surgery 2011; 127(1): 409-13

Discussion by Dennis C. Hammond

Plastic and Reconstructive Surgery 2011; 127(1): 414-6

2. Acknowledgements

3. Abbreviations

3D	Three-dimensional
CCD	Charge-coupled device
CMOS	Complementary metal-oxide-semiconductor
CT	Computed tomography
CTA	Computed tomographic angiography
DECT	Dual energy computed tomography
DIEA	Deep inferior epigastric artery
DIEP	Deep inferior epigastric perforator
DIEV	Deep inferior epigastric vein
DIRT	Dynamic infrared thermography
DSCT	Dual source computed tomography
FDA	Food and Drug Administration
FPA	Focal plane array
ICG	Indocyanine green
ICG FA	Indocyanine green fluorescence angiography
IR	Infrared
LED	Light emitting diode
MDCT	Multi detector computed tomography
MPR	Multiplanar reconstruction
MRI	Magnetic resonance imaging
NIR	Near infrared
NMR	Nuclear magnetic resonance
NSF	Nephrogenic systemic fibrosis
RF	Radio frequency
SIEA	Superficial inferior epigastric artery
SIEV	Superficial inferior epigastric vein
TRAM	Transverse rectus abdominis myocutaneous

4. Summary

This thesis is based on four papers that have imaging techniques used in breast reconstruction as the common denominator. Each paper describes the results of a study. The purpose of the first three studies was to evaluate the use of dynamic infrared thermography (DIRT) as an imaging technique for perforator mapping in breast reconstruction with a deep inferior epigastric perforator (DIEP) flap. The purpose of the fourth study was to evaluate the form stability of the Style 410 anatomically shaped cohesive silicone gel-filled breast implant using magnetic resonance imaging (MRI). The studies reported cover a wide spectrum of imaging methods and all four illustrate how imaging may answer questions raised by the plastic surgeon. The first paper reports an experimental study in a university laboratory, the other three report clinical studies performed in a hospital setting.

DIRT was introduced at the University Hospital North Norway in 2002. It was observed that DIRT could be a promising method for perforator mapping in breast reconstructive surgery with a DIEP flap, but scientific evidence for such use of DIRT was lacking. The results from the first three studies provide scientific evidence to support the use of DIRT in the preoperative planning of DIEP flaps in autologous breast reconstruction. DIRT can replace computed tomographic angiography (CTA), which is today's gold standard, as an imaging technique for preoperative perforator mapping. Such will have great advantages for patients. Unlike CTA, the non-invasive technique DIRT does not require exposure to ionizing radiation or the use of an intravenous contrast medium.

In the fourth study MRI is used in a novel way to visualize the behavior of the Style 410 breast implant in vivo as the body position is changed from supine to prone. The results show that the dimensions of the implant are influenced by the body position. The implant is therefore not form-stable with respect to its dimensions provided by the manufacturer, however, it nevertheless remains anatomically shaped with its largest projection in the lowest pole in both positions. Such knowledge on the behavior of the implant after implantation may help the surgeon in the preoperative planning and provides a better basis for patient information about the possible final result.

All four studies illustrate the value of interdisciplinary collaboration between the radiologist and plastic surgeon. The first three provide scientific support for the clinical use of DIRT as an imaging technique for perforator mapping while the fourth uses the well-established method MRI to answer questions that would otherwise be difficult to answer from the surgeon's clinical point of view.

5. Introduction

In the introduction to his historical book *Radio-diagnosis of pleuro-pulomonary affections*, F. Barjon wrote in 1918: "The physician ought to become interested in radiology. If the radiologist ought to be a physician, it would be well also for the physician to be, in a less degree, a radiologist." [1] Innovation and scientific development are largely dependent on shared interests with colleagues in other specialties, and interdisciplinary collaboration will always be a key to scientific progress, as Barjon also wrote: "Radiology has become a useful science and will become so every day, provided there is a greater collaboration between physician and radiologist." [1]

Almost any conceivable modality or imaging technique within radiology has been used in some way to expand the possibilities and practice of plastic surgery. Derived from the Greek word *plastikos*, which means to be molded or shaped [2], plastic surgery is a discipline that is always seeking creative solutions to solve difficult problems. In many ways, plastic surgery is an art. The plastic surgeon daily makes aesthetic judgments and shapes the human body by remodeling or reconstructing body parts to restore what is missing or malformed. One area where imaging techniques are frequently used is breast reconstruction, which has become one of the major fields of plastic surgery. This thesis is dedicated to the watershed area between plastic surgery and radiology. It is evident that knowledge on plastic surgery is necessary to ask relevant questions. However, some of these questions cannot be answered without knowledge on medical imaging and radiology. During the last two decades, technical development has contributed greatly to the progress of radiology. The radiologist has the necessary knowledge to utilize the possibilities of new imaging technology, and the exploration of watershed areas demands interdisciplinary collaboration.

There are two main aims of this thesis. The first aim is to investigate if there is scientific support for the use of DIRT as an imaging method for perforator mapping and flap planning in autologous breast reconstruction with a DIEP flap. A number of imaging techniques have been used to assist in the selection of a suitable perforator and planning of DIEP flaps. Today CTA is an established method for preoperative mapping of perforators and is considered the gold standard. This method provides information on both diameter and location of the different perforators [3]. Several authors have reported reduced operating time after the introduction of CTA in the planning of DIEP breast reconstructions [4]. However, there are good reasons to develop alternative techniques to CTA. The radiation dose inherently connected to CTA is a major drawback of this imaging modality. Even though allergic reactions to modern contrast media occur quite seldom such an event may be life threatening. The second aim is to investigate the form stability of the Style 410 anatomically shaped cohesive silicone gel-filled breast implant, an implant commonly used in breast reconstruction. The Style 410 implant has been described as form-stable, a characteristic that has been defined as the preservation of identical physical dimensions irrespective of body posture. Information on the behavior of the breast implant after implantation can help the surgeon to predict and improve the postoperative result.

5.1 Breast reconstruction

Breast reconstruction has now become an integrated part in the treatment of breast cancer. Studies indicate that breast reconstruction restores body image with improved vitality, femininity and sexuality as well as positively affecting the patients' well-being and quality of life [5-7]. The goal of breast reconstruction is to restore a breast mould and to maintain quality of life without affecting the prognosis or detection of cancer recurrence. Breast reconstruction can be performed with the use of implants, with the use of autologous tissue, or with a combination of these two techniques.

In breast reconstruction with a DIEP flap, skin and fat tissue is harvested from the lower abdomen. The DIEP flap has become a popular option for women treated with mastectomy for breast cancer. Because no muscle is harvested, there is minimal donor site morbidity at the abdominal wall. The large amount of skin and fat that can be harvested allows for the reconstruction of a naturally looking breast with soft consistency and a volume that may match the contralateral breast. This flap is perfused via a perforator from the deep inferior epigastric artery (DIEA) and vein (DIEV). Vessels with a diameter down to less than a millimeter provide blood circulation to a flap that may have a weight of up to 1 kilogram or more. Selection of a usable perforator is important to secure reliable circulation and avoid necrosis and possible flap loss.

Autologous breast reconstruction demands microsurgical skills and is resource demanding. Many women prefer a simpler solution using a saline or silicone gel-filled breast implant. The main advantages of breast reconstruction with an implant are short operation time and, as there is no need for microsurgical procedure, no risk of flap loss. The use of anatomically shaped implants is claimed to result in increased lower pole fullness of the breast [8-10] and consequently a more naturally looking breast than the use of traditional round implants. Anatomically shaped implants have therefore gained widespread popularity in breast augmentation as well as reconstruction after cancer surgery. The Style 410 breast implant is frequently used in breast augmentation and reconstruction. The manufacturer characterizes the Style 410 as a form-stable implant. Bengtson et al. defined a form-stable implant as an implant that has the same physical dimensions in all body positions [11]. Paper IV provides objective knowledge on the in vivo behavior of the Style 410 breast implant postoperatively.

Although creativity, surgical skills and comprehensive knowledge of anatomy are the most important ingredients of plastic and reconstructive surgery, imaging has become increasingly more important in the planning of reconstructive procedures. Due to the complexity of perforator flap surgery, the distance between success and failure is small. The circulation of perforator flaps relies on the blood supply from a tiny perforator that may have a diameter of less than a millimeter. Although a perforator can be selected intraoperatively without preoperative imaging, this may be very time consuming due to the large variability in the number, location and size of perforators. The extensive dissection required to find a suitable perforator may also increase the risk for vessel damage as inadvertent excessive tension on the perforators may damage these delicate structures. Postoperative flap complications like partial or total flap loss may be the consequences of such damage, as the perfusion of the flap relies solemnly on the blood perfusion through the perforator. These complications are a devastating experience for a patient as they clearly influence the postoperative outcome. Besides the psychological effect such a flap loss may have on a patient, it is also an inefficient use of economical and hospital resources as reoperations are often necessary. Great efforts should therefore be made to reduce the risk for these postoperative flap complications.

With preoperative perforator mapping the surgeon enters known territory when the surgical procedure is initiated. The use of CTA is currently considered the gold standard for perforator mapping and its use has been credited for shortening the operation time [4]. However, disadvantages with CTA are exposure to ionizing radiation and the need for contrast medium injection that can have side effects such as anaphylactic reactions. The first three studies included in this thesis evaluate the usefulness of DIRT in the preoperative planning of breast reconstruction with a perforator flap. The conclusion of this research is that DIRT can replace CTA without the disadvantages of CTA.

MRI is an established method to evaluate the integrity of breast implants. The use of MRI in the fourth study in this thesis illustrates how the radiologist with his knowledge on imaging techniques can contribute to answer questions on the shape and form stability of breast implants used in breast reconstruction.

6. Aims of the thesis

This thesis is dedicated to the watershed area between plastic surgery and radiology. It is evident that knowledge on plastic surgery is necessary to ask relevant questions. However, some of these questions cannot be answered without knowledge on medical imaging and radiology. Summarized for each paper, the aims of this thesis are:

Paper I

To investigate whether the use of DIRT in an isolated perfused human skin flap can provide information on free perforator flap perfusion that is comparable to the information obtained with indocyanine green fluorescence video angiography.

Paper II

To investigate whether preoperative use of DIRT contributes to the selection of a suitable perforator and to the planning of free DIEP flaps in autologous breast reconstruction.

Paper III

To compare the results of DIRT in the preoperative planning of DIEP flaps for autologous breast reconstruction with the results of CTA and hand-held Doppler and evaluate the surgical outcome when perforator mapping is based on DIRT.

Paper IV

To investigate the postoperative shape of the Style 410 implant with MRI and evaluate if the dimensions of the breast implant are influenced by body position during the examination with the intention to evaluate the form stability of the implant.

7. Technology and imaging methods used in the thesis

Technical innovations and new technology are radically changing the daily practice of medical imaging from one decade to the other. Few other medical specialties have harvested so many benefits from the continuing revolution within microelectronics and computer technology as radiology. Even though the general principles of X-rays, ultrasound and MRI remain unchanged, new and creative ways of utilizing these principles emerge with seemingly ever increasing speed.

Many radiologists work in close relationship with engineers, physicists and different experts within technology in the development of new imaging equipment, software and interventional procedures. For radiologists who are interested in exploring new technology, the possibilities for exciting research and development of new imaging methods are almost unlimited. However, close collaboration between radiologists and other medical specialties is also essential to exploit novel clinical applications for new imaging technology.

For more than a century there has been such fruitful collaboration between radiologists and other physicians, and nobody could have imagined the revolutionary developments that have taken place within the field of radiology during the last 100 years. Almost the whole electromagnetic spectrum is used in medical imaging from radiofrequency pulses in MRI to gamma rays in nuclear medicine, and high frequency mechanical vibrations are utilized in a vast range of advanced ultrasound equipment.

In the following sections we will have a look at the historical development of radiology and its implications for medicine in general and plastic surgery in particular. It is a history of innovation and collaboration, not only between radiologists and other physicians, but also with engineers, physicists and scientists in a wide range of scientific disciplines working together for the progress of medical imaging.

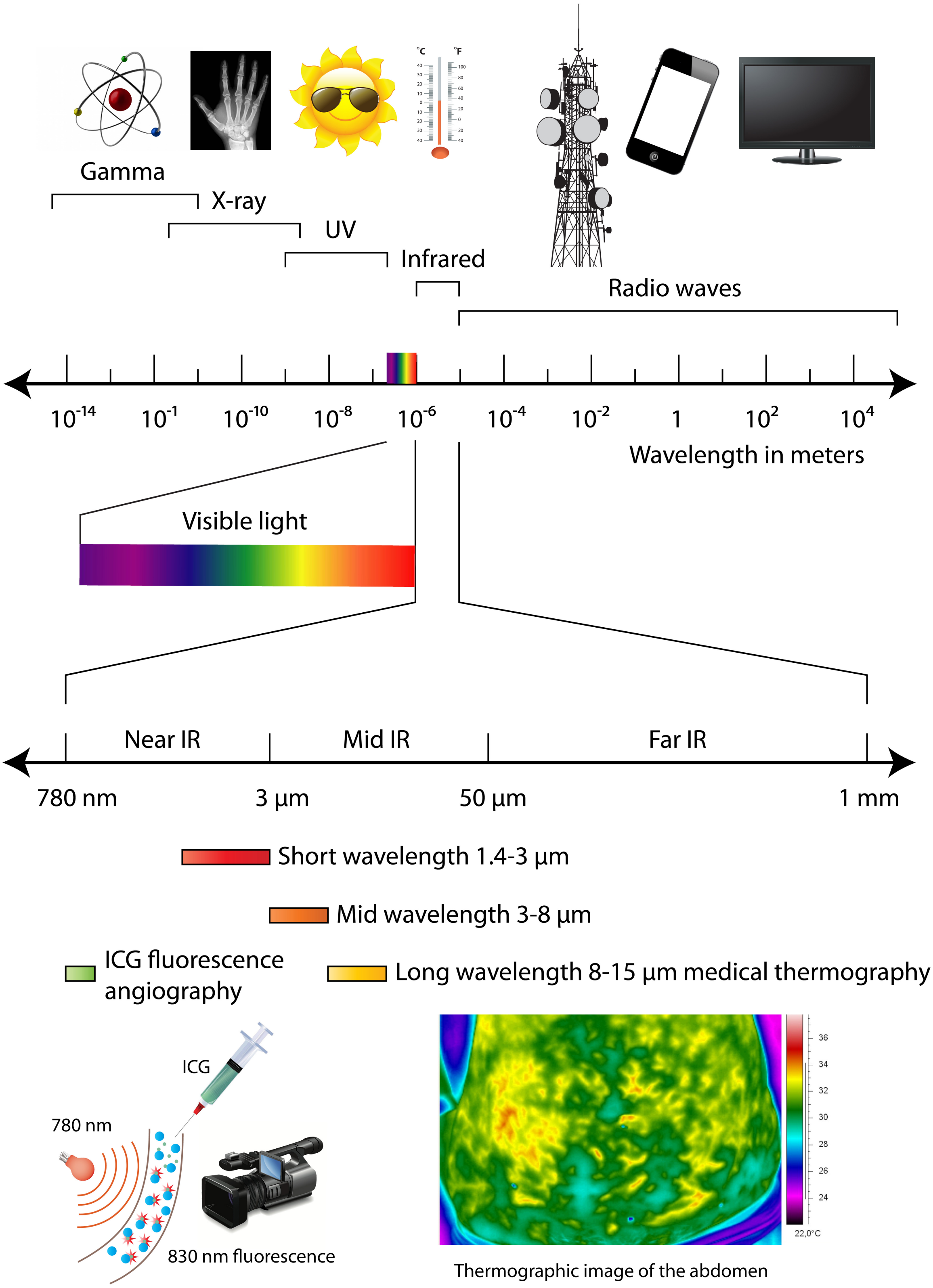

Figure 1 Almost the whole electromagnetic spectrum is used in different types of medical imaging from radio frequency pulses in MRI to gamma rays in nuclear medicine.

7.1 X-ray and conventional angiography

The history of radiology started with the epoch-making work of Wilhelm Konrad Röntgen. He was studying the phenomena accompanying the passage of electric current through a vacuum tube, and on the evening of November the 8th 1895 he discovered the rays that would later be named after him. He observed that a vacuum tube connected to high voltage would cause fluorescence of a piece of barium platinocyanide paper. The vacuum tube was encased within a close-fitting shield of black paper to exclude visible light, proving that this was another kind of radiation than light. In his legendary article *On a New Kind of Rays,* Röntgen reported a huge amount of experiments describing the physical properties of the radiation he called X-rays [12]. Fluorescence was visible at a distance of two meters, and he observed that all bodies were transparent to X-ray in varying degrees. "If the hand be held before the fluorescent screen" Röntgen wrote, "the shadow shows the bones darkly, with only faint outlines of the surrounding tissues". He also described the fact that photographic plates are sensitive to X-rays. In 1901 Röntgen received the Nobel Prize in Physics for his discoveries [13].

Almost immediately physicians and physicists all over the world began to work on the development of X-ray equipment for medical use. This new possibility of visualizing anatomy and pathology in vivo was revolutionary to diagnostics as well as medical research. During the next 50 years X-ray technology went through dramatic improvements including the development of better X-ray tubes, high voltage generators, photo-timers for exposure control and films combined with fluorescent screens that vastly increased the sensitivity and quality of examinations. During the same period new techniques such as *stereo-roentgenography* for 3D X-ray acquisition, *planography* for body section radiography, *kymography* for the visualization of physiological movements and *photofluorography* for image acquisition on small format film were developed [14].

Radiographic examinations have been used in surgery since the very beginning. As early as in 1896, the American surgeon James Burry reported on the successful use of a roentgenogram to locate and remove a small piece of buckshot from the hand of a painter. Professor of Surgery Carl Beck wrote an important textbook on fractures and the clinical use of X-ray, and in 1904 he published his textbook *Roentgen Ray Diagnosis and Therapy* [15].

In the early days bone and foreign bodies provided tissue contrast. With the use of oral contrast agents like bismuth nitrate (and later barium sulphate) the alimentary tract could be studied. The first account of an angiogram involved the injection of *Teichmann's mixture*, a solution of lime, cinnabar and petroleum into the hand of a cadaver [15]. In the early 1920s, Egas Moniz injected sodium iodide directly into the internal carotid artery to produce an X-ray image of the cerebral circulation. Unfortunately, the patient died from status epilepticus [16], but the quest for safer contrast media continued. In 1927 the first commercially available intravenous contrast medium was developed and marketed by Schering for urinary tract radiography [17]. The introduction of intravenous contrast media opened the era of angiography, making the visualization of arteries and veins possible. For plastic surgery, angiography was an important tool that could provide new understanding on vascular malformations, skin circulation and optimal flap design.

The Swedish radiologist and angiography pioneer Sven Ivar Seldinger revolutionized interventional radiology by introducing a new method for the introduction of catheters into vessels [18]. In his article from 1953 Seldinger wrote: "The main principle consists in the catheter being introduced on a flexible leader through the puncture hole after withdrawal of the puncture needle" [19]. Today this technique is used by radiologists all over the world, enabling access to almost any vessel in the body through arterial or venous access far away from the vessel of interest.

In plastic surgery, as in almost all medical specialties, X-ray technology is widely used in both clinical work and research. One example of research is the work done by Robert Hamas for radiographic visualization of the shape of breast implants in vivo [20]. However, the most significant contribution by radiographic techniques to plastic surgery is in the research area of vascular anatomy and the development of new operative techniques.

In 1889 Manchot, at the age of 23, a few years before the discovery of X-rays, published his pioneering work *Die Hautarterien des menschlichen Körpers*. Almost a century later in 1983 his work was published in English as *The Cutaneous Arteries of the Human Body*. Manchot described the cutaneous perforators and their source vessels, and based on his dissections he even described different cutaneous vascular territories. The development of radiography provided new possibilities for vascular research. In the 1930s Michel Salmon injected entire cadavers with a mixture containing lead oxide and examined the bodies with X-ray. He mapped the entire cutaneous circulation as well as the blood supply of every muscle in the body. He published his work in French in 1936 but it was not available in the English language until 1988 [21]. Based on the research by Manchot and Salmon, Taylor and Palmer published in 1987 a large study on vascular territories in cadavers [22]. They used ink injections with dissections and radiographic analysis of fresh cadavers. Their *angiosome concept* describes a continuous three-dimensional network of vessels in the skin and deeper tissue layers. Their research showed how arteries closely follow the connective tissue framework of the body. The skin is primarily supplied by cutaneous arteries, which vary in caliber, length and density in different regions. The angiosome concept has provided a major contribution to the understanding of tissue circulation and the development of flap surgery.

In 1945 Morgan and Lewis wrote: “Until the present time roentgenology has constituted one of the most dynamic of the medical sciences. There is little reason to believe that it will ever be other than progressive and fruitful of significant achievements.” [14] They were right in their belief as radiology has gone through even larger progress with the development of new modalities and advanced imaging techniques. And still conventional X-ray technology plays an important role in the daily clinical practice and scientific research of plastic surgery.

7.2 Computed tomography

Conventional radiography is a valuable tool that is still responsible for the largest number of examinations in most radiology departments. However, traditional X-ray examinations have several drawbacks that limit their ability to visualize low-contrast tissues and three-dimensional (3D) information. Due to the large X-ray beam used in conventional radiographic examinations, scattered photons represent at least 50 % of the radiation absorbed by the film or digital detector [23]. Scatter creates background intensity in the image that does not relate to the visualized anatomy. These drawbacks were overcome with the introduction of computed tomography, or plainly CT.

The British engineer Godfrey Hounsfield at EMI Laboratories was interested in optimizing systems to utilize all available information. In his legendary article in *British Journal of Radiology* published 1973, he wrote: "In the conventional film technique a large proportion of the available information is lost in attempting to portray all the information from a three-dimensional body on a two-dimensional photographic plate, the image superimposing all objects from front to rear." [24] He then described the world's first CT system. The X-ray tube, detectors and collimators were fixed on a common frame with the tube and detectors placed on each side of the patient's head. The frame was systematically rotated around the head, taking 160 readings between every rotation of one degree. A total of 28.800 readings were stored in a disc file for processing by a computer. By calculating 28.800 equations with 6.400 variables, the computer was able to produce a matrix of 80 x 80 numerical values representing the degree of X-ray absorption by a similar matrix of anatomic locations within a slice through the patient's head. The values were printed as numbers on a line printer and viewed on a cathode ray-tube as pixels with gray tones reflecting the numerical values. Six axial images were made during a period of 35 minutes per patient.

Even though the images produced by Hounsfield's CT system were extremely coarse compared to those made with modern scanners, this was a huge improvement in comparison to conventional radiography. According to Hounsfield, the values of the absorption coefficients of various tissues were calculated to an accuracy of 0.5 %. Within the brain, the tissue absorption values found in different tissues including cerebrospinal fluid cover a 4 % range. By adjusting image contrast and brightness so that this 4 % range, also called *window*, covered the whole gray scale from black to white, different tissues of the brain could be visualized on the screen. Hounsfield constructed a scale with absorption values where air was given the value -500, water 0 and bone approximately +500. Later the values were doubled to cover -1000 to +1000, water still having an absorption value of zero. Nowadays this scale is used by radiologists all over the world, and the values are named *Hounsfield units* after their inventor.

In 1979 Allan Cormack and Godfrey Hounsfield were given the Nobel Prize in Medicine or Physiology for inventing the CT scanner. “Cormack had been working on the concept of scanning slices of the body from various angles and rotations. But it was Hounsfield’s work on pattern recognition and the use of computers to analyse readings that made the CT scanner possible”, *The Lancet* wrote in their obituary article when Hounsfield died in 2004. In the same article, professor emeritus and RSNA president Brian Lentle was cited saying: “I think when people saw the very first CT images – and they were, by modern standards, not great images – whenever any of us saw those images we realised that radiology was never going to be the same again.” [25]

The history of radiology would go on for 76 years from the discovery of X-rays to the first clinical CT images were made in 1972 [26], and radiology has never been the same since. During the following 40 years, there have been many revolutionary technological improvements to CT that have benefited clinical practice and provided new possibilities for scientific research.

The first CT scanner was only able to scan the head. The patient had to lie still for 35 minutes in the scanner, and a rubber cap surrounded with water was covering the patient’s head. In 1974 the first body scanner was introduced that enabled imaging of the whole body without the need for water surrounding the scanned part of the body. New hardware and more efficient computer algorithms for image reconstruction vastly reduced scanning time and increased image quality. Subsequent generations of scanners used several different scanning techniques and numbers of detectors. A breakthrough for scanner speed came with the introduction of the low voltage slip ring in 1987 [23]. Until that time, cables connecting the rotating parts of the scanner required that the rotation stopped after each rotation and reversed its direction. Scanning, braking and reversing took 8-10 seconds while only 1-2 seconds were used for data acquisition.

With the introduction of the slip ring, electrical power and signals could be transferred without fixed connections, making continuous rotation of the X-ray tube and detectors possible. In spiral CT, or helical CT, the examination table is smoothly moved through the gantry during the examination. In this way, data is collected in a spiral shaped path allowing much shorter scanning times. Spiral CT has been available since 1989 [27]. The shortened scan time allowed larger parts of the body to be examined in a single breath hold and entire areas to be scanned within the vascular enhancement phase after intravenous contrast injection [28]. With this new technology, CT angiography (CTA) became an alternative to conventional angiography. With CTA both large and small vessels may be visualized in spite of the fact that contrast medium is injected in a peripheral vein and not via selective catheterization.

Even though configurations of several X-ray detectors had been used in CT scanners for many years, it was not until 1998 that the so-called multi-slice, or multi-detector CT (MDCT) scanner, was introduced [27]. In earlier CT scanners, all detectors were used for image acquisition within one single slice of the body. In MDCT scanners several detectors are used in the longitudinal direction allowing the continuous acquisition of several parallel slices. Modern scanners may have up to 320 parallel detectors at 0.5 mm covering an area of 16 cm that may be scanned in 0.35 seconds [29]. In this way a larger anatomical region as for instance the whole heart may be visualized in one single rotation without even moving the examination table.

The short scanning time and high spatial resolution of MDCT provided many new possibilities for CT scanning. Even 16-slice MDCT, which has now been available for a decade, provides an isometric spatial resolution of less than one millimeter, which makes detailed 3D reconstructions of organs and even small contrast-filled vessels possible. With the newest MDCT scanners an isometric resolution down to 0.3-0.4 mm is achievable.

In recent years dual-energy CT (DECT) has also become available. Modern DECT scanners are dual-source CT (DSCT) scanners with two X-ray tubes and two sets of detectors mounted on a CT gantry with 90 degrees offset. One great advantage with these scanners is that the combination of two sets of tubes and detectors makes it possible to obtain a complete volume acquisition in one quarter of a gantry rotation. This means that with a 0.33 second rotation time, a volume may be captured in only 83 milliseconds. Such temporal resolution is ideal for cardiac imaging because motion artifacts due to cardiac movement can be omitted. In addition, so-called dual energy information may be obtained if the two X-ray tubes are operated with different voltage [30].

Figure 2 Modern MDCT and DECT scanners provide new and exciting diagnostic possibilities. With no table movement the patient's heart may be scanned in a fraction of a second. The first DECT scanner in Northern Norway was a donation from Trond Mohn.

In his article published in 1973 Hounsfield also described the principle of DECT scanning: "It is possible to use the machine for determining approximately the atomic number of the material within the slice. Two pictures were taken of the same slice, one at 100 kV and the other at 140 kV. If the scale of one picture is adjusted so that the values of normal tissue are the same on both pictures, then the picture containing the material with high atomic number will have higher values at the corresponding place on the 100 kV picture. One picture can then be subtracted by the other by the computer, so that areas containing high atomic numbers can be enhanced." [24]

Modern DSCT scanners do this process with two separate X-ray tubes at the same time, and the software can then remove for instance calcium or contrast medium after acquisition. Pre-contrast images may be artificially constructed from images taken with intravenous contrast by subtracting the attenuation created by the contrast medium. This is one way of reducing radiation dose to the patient, as pre-contrast scanning in some cases may be omitted. In the same way, bone may be artificially removed from the pictures for better visualization of soft tissues and vessels. The same technique may also be used to differentiate between kidney stones and gallstones of different chemical constituents [30].

The high isometric spatial resolution of CTA provides many possibilities for the visualization of small vessels used in reconstructive surgery. With 3D and multi-planar reconstructions (MPR) CTA may provide detailed visualization of vascular anatomy and 3D models of large vessels as well as tiny perforators. Modern post-processing software is easy to use and provides almost endless possibilities for MPR and 3D reconstructions. While such software packages used to be expensive and provided by the industry, many open source alternatives are now available. In the study reported in paper III, the open source DICOM viewer OsiriX was used in the reading and reconstruction of CTA images. For research purposes this free version of OsiriX may be used on any Mac computer running OS-X. A commercially available version, called OsiriX MD, is approved by the FDA diagnostic imaging in medicine. It is our experience that OsiriX is very user-friendly and that it provides excellent reconstructions that are as good as, or in some cases even better than, those provided by commercially available software, an experience shared by other researchers [31-33].

7.2.1 CTA and breast reconstruction with a DIEP flap

Today CTA is an important tool in research on vascular anatomy and provides valuable information that can be used for flap surgery. While cadaveric studies have contributed largely to our knowledge on vascular anatomy, CTA visualizes the vessels in vivo and is not influenced by possible post mortem changes to the anatomy. In breast reconstruction with free DIEP flaps based, CTA has been an important tool in visualizing perforators and classifying different branching patterns of the deep inferior epigastric artery (DIEA) [34]. Rozen et al. compared the results of anatomical dissections of 45 cadaveric hemi-abdominal walls with the results obtained after injection of contrast medium in the DIEA and subsequent CTA [35]. Such research has provided increased understanding of the course of perforators through the rectus muscles and the relationship between different DIEA branching patterns and the size of perforators.

The *angiosome concept* introduced by Taylor and Palmer in 1987 was based on their cadaveric studies with dissection, dye injections in vessels and conventional radiography after intravascular contrast injection of the specimens. The importance of their contribution to the understanding of flap harvesting and survival is indisputable. Perforator flaps are now widely used in reconstructive surgery. An increased understanding of the vascular territory of the single perforators has been provided with the use of CTA. Saint-Cyr et al. introduced the *perforasome theory* in 2009 [36]. Using 40 fresh cadavers a total of 217 flaps and arterial *perforasomes* were studied. The authors define the term perforasome as the vascular territory of a single perforator. In their article, they used dissection with methylene blue dye injections and CTA with 3D reconstructions of the perforators in the abdominal wall to reveal the vascular territories of individual perforators. They also showed how adjacent perforasomes are linked with adjacent perforasomes by direct and indirect vessels. The same group used what they called “three- and four-dimensional CTA” to study abdominal flaps used in breast reconstruction [37]. They injected contrast medium at a constant flow in each artery or perforator and CT scans were repeated with time intervals of 15 seconds during the first two minutes, then every 60 seconds for the next two minutes. 3D reconstructions of the progressive CTA were used to analyze branching patterns and to measure vascular territories.

As reported in paper I, 8 abdominal flaps harvested during abdominoplasty were used in a study comparing ICG FA with DIRT in their ability to visualize skin perfusion. During individual perfusion of 19 selected vessels with warm and cold fluid the flaps were monitored with an infrared camera. The same vessels were perfused with ICG, and ICG FA was used to visualize fluorescence from the vessels. In each flap a selected vessel was also perfused with iodinated contrast medium for X-ray imaging. The X-ray images were used to visualize the position of major veins and confirm the position of catheters used in the perfusion of the selected vessels. Although not described in the paper, all flaps were also examined with CTA after the experiment for visualization of the vascular anatomy within the flaps. Preliminary results including 3D CTA images were presented at the annual meetings of the Norwegian Association for Plastic Surgeons [38] and the Norwegian Association of Radiology in 2006 [39].

In 2006 Masia et al. reported the use of 16-slice CTA in the preoperative planning of DIEP breast reconstruction in 66 patients [40]. They registered neither false positive nor false negative results in the outcome of CTA compared with intraoperative findings. CTA was used to identify the three best perforators on each side of the abdomen. 3D reconstructions were used to locate the points on the skin surface where the three best perforators emerged from the fascia of the rectus abdominis muscle. To report these locations, a virtual coordinate system with the umbilicus at the center was used. According to their article, valuable time could be saved during surgery as CTA provided the opportunity for the surgeon of going directly to the best perforator without performing an extensive dissection to get an overview of all possible perforators.

The same year Alonso-Burgos et al. reported on the successful use of CTA in the preoperative planning of DIEP breast reconstruction in six patients [41]. They obtained accurate identification of the main perforators in all patients with “very satisfactory concordance” between MDCT angiography and surgical findings. In their study they used a four-slice CT scanner and made MPR, maximum intensity (MIP) and 3D volume rendered reconstructions to evaluate the location of perforators, their origin, course and anatomical variations. According to their article, “no CT-unreported vessels were found during the surgical procedure”.

In 2007 Smit et al. compared the results of using CTA with the use of only hand-held Doppler in the planning of DIEP breast reconstructions. 70 patients were examined with 16-slice CTA and 68 with hand-held Doppler. They reported a significant reduction of operative time (average 90 minutes reduction for unilateral reconstruction) and a tendency for fewer complications in the CTA group. However, the difference in complication rates was not statistically significant. Uppal et al. compared 26 patients operated with preoperative CTA perforator mapping with patients operated prior to the introduction of CTA [42]. They found that the average operating time was reduced with 76 minutes and therewith also a considerable cost reduction.

In 2009 Casey et al. reported on operative times and postoperative outcomes before and after routine use of preoperative CTA in breast reconstruction with a DIEP or superficial epigastric artery (SIEA) flap [4]. Of 287 flaps in 213 patients, 101 flaps were examined with CTA whereas 186 flaps were examined with only hand-held Doppler in the preoperative phase. According to their results, there was strong correlation between CTA and the intraoperative findings. The introduction of CTA lead to decreased operative times and reduction of abdominal bulges postoperatively. However, no significant reduction of anastomotic complications, flap failures, fat necrosis or abdominal wound complications, were found. They concluded that CTA might increase surgeon comfort with the procedure and reduce the steep learning curve for surgeons learning to perform these technically demanding operations.

The SIEA flap has several advantages when compared to the DIEP flap, as the flap dissection is less complicated and the procedure is associated with less donor site morbidity because the harvest of a SIEA flap does not involve a dissection through the rectus abdominis muscle. However, not all patients have an adequate SIEA and superficial inferior epigastric vein (SIEV) to provide blood supply to a reconstructed breast. Piorkowski et al. used CTA in the preoperative planning of 177 free flaps used for breast reconstruction in 113 patients [43]. Of the patients included in their study, 43 % had at least one visible SIEA on CTA, while only 21 % had a SIEA considered adequate for breast reconstruction on CTA. This corresponded well with the findings of Masia et al. reporting 62 % of the patients having at least one visible SIEA on CTA, of which 24 % were considered to be considered adequate for surgery and 19 % were actually used by the surgeon to supply a flap [44].

In our own institution we have used CTA in the preoperative planning of perforator surgery for several years. In paper II, the usefulness of DIRT in the preoperative planning of perforator flaps was evaluated based on the intraoperative findings and postoperative results. In 8 patients CTA was performed to see if the results obtained with DIRT could be related to the findings on CTA. In our experience CTA provides detailed information on the branching pattern of the DIEA on both sides, the existence of a SIEA as well as the localization and size of individual DIEA perforators. There is however, concern about the radiation dose inherently correlated to CT examinations.

There is no doubt that CTA has become a valuable tool in the preoperative planning of perforator flap surgery. CTA provides information on DIEA branching pattern, the presence or absence of a SIEA as well as the distribution and diameter of different perforators. However, as Cina et al. have shown, we cannot always separate between the perforator artery and vein [45]. CTA can be performed as a multiphasic examination, which would provide dynamic information about flow in the perforators. However, such a multiphasic examination increases the radiation dose considerably. With the standard CTA a static picture of the vessels is obtained. The diameters and degrees of attenuation reflecting the concentration of intravascular contrast medium of the different perforators are compared at a certain point of time.

Even though many consider CTA as the preferred modality for all patients undergoing perforator flap surgery, there are several alternatives that may complement or even substitute CTA in this area. Color Doppler is an operator dependent and time-consuming examination but provides accurate information on the location, diameter and flow of individual perforators. Dynamic MRI may also become an important alternative to CTA in the preoperative planning of perforator flaps. Even though MRI may not have the same spatial resolution in the evaluation of all perforators, multiple acquisitions may be performed to obtain dynamic information on flow without the use of ionizing radiation. Although the use of DIRT as an imaging technique for perforator mapping in DIEP flaps was already described in 1993, it has not gained widespread popularity. DIRT does not provide detailed anatomical information, but allows for a dynamic evaluation of each perforator's location and function through analysis of the rate and pattern of rewarming at the hot spots. One of the reasons for its lack of popularity could be that DIRT provides only indirect information on skin perfusion by measuring skin temperature. Skin temperature is not only influenced by heat radiation from local blood flow but also from metabolic processes and from deeper tissue [46, 47].

However, there is no reason to believe that CTA will disappear as a useful imaging method for perforator mapping. New scanners with a high number of detectors and dual energy technology may provide many new possibilities for detailed anatomical mapping in combination combined with reduced radiation dose to the patient. Today we have more diagnostic tools available than ever before. More than relying on using the same tool for every job, it may be profitable to have a larger toolbox and choose the right tools in every individual case.

7.3 Ultrasound and Doppler

In 1773 the Italian scientist Lazzaro Spallanzani observed that blind bats could fly and avoid obstacles as well as bats that could see. Five years later Charles Jurine found that when the ears of bats were plugged with wax, the otherwise superb navigators became helpless and collided with obstacles [48]. More than 150 years passed until Galambos and Griffin used an ultrasonic detector to show that bats navigated by emitting ultrasound and receiving the echoes [49].

Figure 3 Bats effectively use echolocation with ultrasound pulses for navigation and hunting (Photo: Colourbox.com).

In much the same way as bats and dolphins use ultrasound in navigation, ultrasound pulses are used in medical imaging to visualize anatomy and pathology in the human body. The first ultrasound diagnostic systems were developed for industrial use. Prior to the development of ultrasound technology, X-rays were used to control the integrity of ships' metal hulls. The American researchers Sproule and Firestone pioneered the necessary technology for using ultrasound in the megahertz range with ultrasound pulses having durations as short as microseconds. Their technology was developed in 1941 but could not be published until after the war in 1946 [50]. With their equipment tiny defects in steel constructions could be revealed by ultrasonic examination.

During World War II, the English surgeon John Julian Wild cared for many patients with paralytic ileus caused by blast injuries from German bombing. Wild found it difficult to distinguish between paralytic ileus and obstruction and came up with the idea of using ultrasound in the diagnostics. After the war, he moved to America and was employed at Owen H. Wangensteen's laboratory in Minnesota [50]. Wild used a 15 MHz military transducer and was able to measure the thickness of the bowel wall. He was even able to visualize three distinct layers of the intestine in a large water tank [50]. He used so-called A-mode, or *amplitude mode*, which is the simplest form of ultrasound imaging. After transmitting a short ultrasound pulse into the body, the transducer was listening for echoes that were visualized as peaks with varying amplitude on an oscilloscope's cathode ray screen.

Using ultrasound equipment originally made by the U.S. Navy during World War II for the simulation of radar, Wild did several pilot studies on the echo-producing properties of biologic tissue [51]. He observed a striking difference in echo-patterns in carcinomatous ulcers, brain tumors and breast cancer when compared to normal tissue. While other equipment used for ultrasound operated on lower frequencies with relatively low power, this military equipment was able to produce pulses at a frequency of 15 MHz with a peak power of 644 watts per square centimeter. However, the duration of the pulse was only one-half millionth of a second, giving an average intensity that was not more than 1.3 watts per square centimeter. Wild and his coworkers did not observe any unpleasant side effects of ultrasound examination or pathological changes in tissues that had been examined with the machine he named *the echograph* [51].

With the development of B-mode ultrasound, the spikes on the oscilloscope were exchanged with a two-dimensional array of bright and dark spots on a cathode ray screen. Instead of visualizing the amplitude of echoes as peaks on a line, several lines were put together with the brightness of each image component reflecting the amplitude of a single echo. For the generation of B-mode images, Wild used a hand-held instrument with a propagating crystal that scanned to and fro over a range of 6.5 cm within an elliptical water-chamber [52]. Wild developed scanning devices not only for breast cancer screening, but also trans-rectal and trans-vaginal transducers [50].

In 1952 Wild wrote about A-mode and B-mode: "The echographic structures of tissues can be obtained in one dimension, in a manner analogous to a needle biopsy, or in two dimensions, in one plane. Accordingly, the concepts of uni-dimensional and two-dimensional echography can be introduced" [51]. He even wrote that "further developments could produce three-dimensional echography", a technology that recently has become available in commercially available ultrasound machines. Far ahead of his time, Wild also wrote that "it should be possible to detect tumors of the accessible portions of the gastrointestinal tract both by density changes and also in all probability, by failure of the tumor tissue to contract and relax" [50]. Nowadays, these principles are used in modern ultrasound diagnostics with elastography.

While Wild concentrated on the clinical use of ultrasound, Douglass Howry was working on the development of new equipment. In contrast to Wild who was a surgeon, Howry had a background in radiology. Howry's ultimate goal was to make images "in a manner comparable to the actual gross sectioning of structures in the pathology laboratory" [53]. Between 1948 and 1952 Howry and Wild, in spite of being unaware of each other's work, both developed methods for producing cross-sectional images with the help of ultrasound. Howry and his collaborator Bliss who was an engineer, constructed their first B-mode ultrasound scanner from surplus naval sonar equipment [54]. The patient's body and the transducer had to be submerged under water during the examination. In 1954 Howry and Holmes constructed a B-mode scanner they called *the Somascope*. In this construction they used a surplus rotating ring gear from a Boeing B-29 gun turret to rotate the transducer 360 degrees around the patient [50]. The Somascope produced images with reasonable quality, but as the patient had to stay motionless with the body submerged in a water tank, the machine was impractical for use in clinical settings.

During the first years of the 1950s many researchers around the world worked on the development of ultrasound diagnostics. In Sweden the cardiologist Inge Edler and the nuclear physics graduate student Carl Hellmuth Hertz at Lund University measured heart activity using ultrasound equipment borrowed from a ship construction company in Malmö. Edler later made echoencephalograms of the brain and developed the technique of echocardiography of the heart [15]. In 1957 Effert and colleagues used ultrasound to visualize the movement of the left atrial walls simultaneous with electrocardiography and phonocardiography in the relative assessment of mitral stenosis and incompetence [52].

In Scotland the obstetricians Ian Donald and John MacVicar worked with the physicist Tom Brown to modify industrial ultrasound equipment for use in medical diagnostics. Donald was a veteran of World War II and humbly said about himself that he had "rudimentary knowledge of radar" from his days in the Royal Air Force and "a continuing childish interest in machines, electronics or otherwise – or what my wife would refer to as my "toys"" [55]. He knew the work of Howry who according to Donald "ran into difficulties because of the need to immerse the naked body of his subject in a large tank of water". Donald was given the opportunity of borrowing an ultrasonic metal flaw detector to see if he could discern any differences in ultrasound echoes from varying types of pelvic tumors. "I shall always remember that lovely sunny afternoon of the 21 July 1955 when we took down the factory in Renfrew two cars with their boots loaded with recently excised fibroids, small, large and calcified, and a huge ovarian cyst" Donald wrote [55]. "The people in the factory had also supplied an enormous lump of steak by way of a control material. There then followed a series of fascinating experiments behind closed doors in their research department".

John MacVicar joined Donald's staff in 1956 and helped greatly with the development of new ultrasound probes with barium titanate that could be applied directly to the patient's abdominal wall through a film of olive oil. Using A-mode they examined hundreds of patients, "but we earned great mockery from our colleagues who naturally suggested that digital palpation was surely good enough" Donald wrote [55]. Their breakthrough came when they were asked to examine a supposedly dying woman with massive ascites due to portal obstruction from a radiologically demonstrated carcinoma of the stomach. The metal flaw detector demonstrated echoes that had to come from a large cyst, and the radiological findings were declared to be an artifact. A massive mucinous cyst was removed from her abdomen, and the patient's life was saved [55]. One year later they started using ultrasound to study pregnancy and measure the fetal head size. In 1957 they also developed a new B-mode scanner. In their legendary Lancet article published in 1958, Donald et al. described the principles of ultrasound diagnostics with A- and B-mode, illustrated with cases covering various conditions of pregnancy, ovarian cysts, fibroids, ascites and a complicated ovarian tumor [52].

Today the word Doppler is familiar to all who are involved in the practice of medicine. We cannot even imagine using an ultrasound machine without different options for Doppler imaging, which relies on a fundamental physical principle discovered by Christian Johann Doppler in 1842. He discovered the effect that has been named after him by observing ships on the sea and said that "nothing seems easier to understand than the distance and time interval between two successive waves must become shorter for an observer, who is hurrying towards the source of the waves, and longer if he is moving away from it" [56]. In 1845 Christoph Hendrik Diederik Buys Ballot conducted an elegant experiment that proved the truth of Doppler's theory. A group of trumpet players were positioned on a train wagon blowing a constant tone as the train passed a group of observers. The observers could verify that the pitch of the trumpets was higher when the train approached them and lower as the train drove away. Doppler was primarily focused on astronomy and the movement of stars and could not have imagined the impact his theory would have on future science and technology. Today the Doppler effect is used not only in astronomical studies, but also in microscopic spectroscopy, radar equipment in satellites and airplanes, direction finding systems and police equipment for speed control in addition to diagnostic ultrasound [57].

The first application of the Doppler effect in medicine involved measurement of different transit times of ultrasound travelling through flowing blood in different directions. Using this principle, Hebry P. Kalmus made an electronic flowmeter in 1954. The

Japanese physicist Shigeo Satomura published an article in 1956 reporting that cardiac valvular motions could be registered with the use of Doppler signals, but his work was only published in Japanese and was therefore unknown in the West [50].

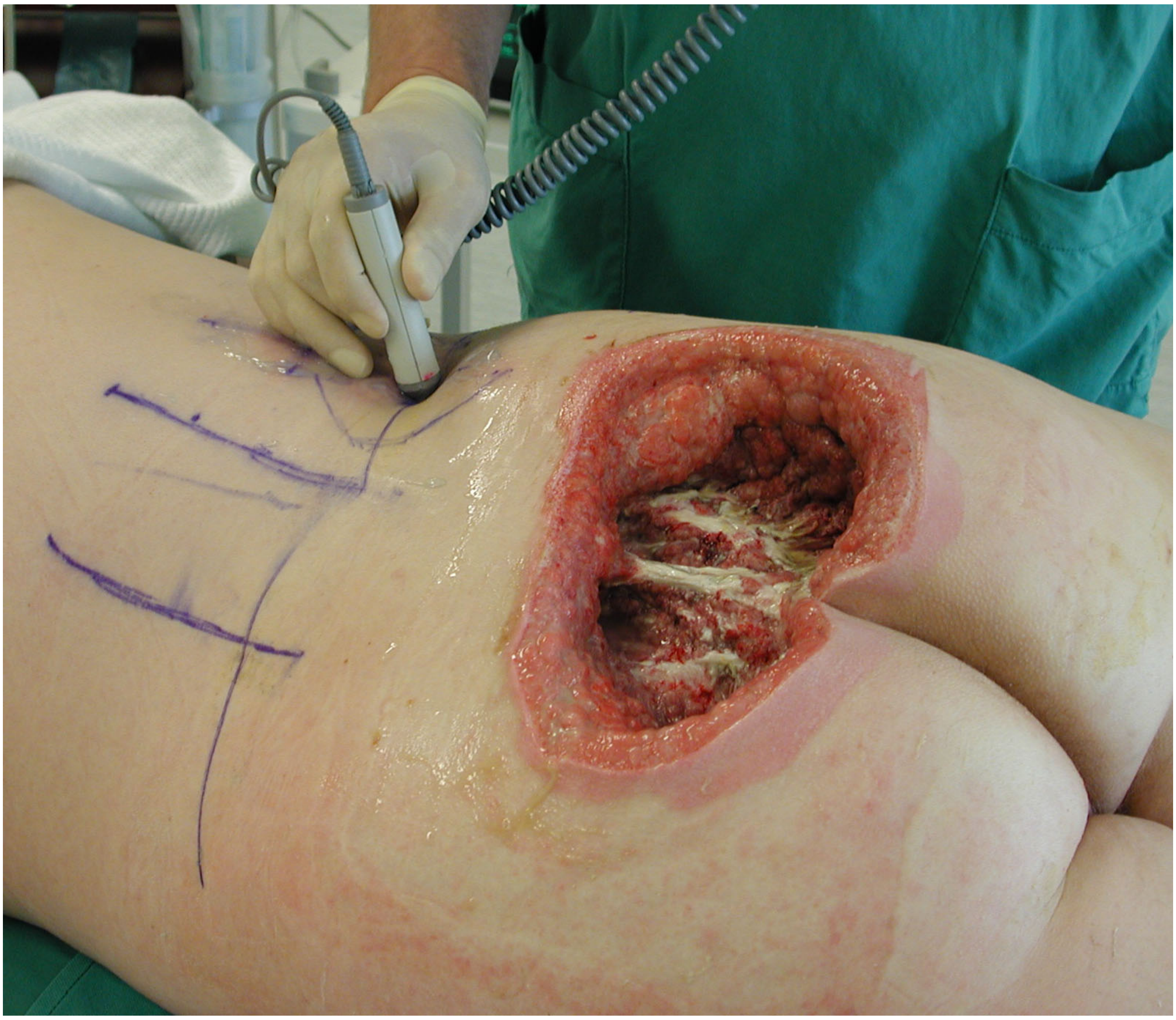

Figure 4 Hand-held Doppler is widely used in the evaluation of arterial perforators. This patient had a large pressure sore that was operated with *The Butterfly Design* using two flaps based on lumbar artery perforators [58].

In 1961 Franklin, Schlegel and Rushmer published a short article in Science with the title *Blood flow measured by Doppler frequency shift of back-scattered ultrasound* [59]. In this article they described the simple principle of using the Doppler shift of a continuous ultrasound source to measure blood flow within vessels. Their instrument had two piezoelectric crystals in a plastic cylinder. One of the crystals emits continuous ultrasound at a constant frequency of 5 MHz while the other crystal is used as a receiver. Ultrasound transmitted into a blood vessel is reflected by the blood cells and registered by the receiver crystal. Due to movement of the blood cells, the reflected signal has a slightly different frequency than the transmitted signal according to the Doppler effect. The received signal is amplified and mixed with the transmitted signal to develop a beat signal corresponding in frequency to the Doppler shift. In a *hand-held Doppler* device, this beat signal is sent to a loudspeaker, making arterial and venous flow audible to the ear.

Strandness et al. described the use of a commercially available hand-held Doppler in 1967 [60]. The instrument had a portable main unit connected to a small hand-held transducer, which could be used externally on the skin to assess qualitative information on the velocity of arterial and venous flow. Because of its portability and convenience in operation, the instrument could be easily transported from the laboratory to the bedside, operating room or clinic. In their article, Strandness et al. report the successful use of hand-held Doppler in 84 cases of arterial disease like occlusion, arteriosclerosis and fistulae as well as 17 cases of venous disease like thrombophlebitis, evaluation of extremity edema and monitoring of venous flow after thrombectomy or inferior vena cava ligation.

A prerequisite for spectral Doppler and color Doppler is the use of pulsed-wave Doppler signals. Baker et al. started their work on pulsed-wave Doppler in 1966 and were among the first to produce such an instrument in 1970 [50]. This team also constructed a mechanical transducer that combined real-time imaging with Doppler functions. In 1976 Baker and his coworkers described techniques for spectral analysis using Fourier transformation performed in real time by a computer to determine if blood was flowing toward or away from the transducer [61]. Graphic curves showing the flow velocity and direction were used to reveal the presence of plaques, intrusions and complete occlusions. In the last paragraph of the article Baker et al. wrote: “When the two methods are combined with a superimposed sound beam vector on the flow image display it may be possible to compute the intervening angle” thereby making quantitative flow measurements possible. Today such functions are integrated in almost all ultrasound machines. Spectral Doppler is instantly available at the push of a button. In color Doppler imaging blood flowing towards and away from the transducer is visualized as respectively red and blue color superimposed on the B-mode picture.

In 1972 Goldberg and Pollack published an article in *Radiology* about their “ultrasonic aspiration transducer” [62]. By drilling a hole in a 2.25 MHz transducer they used A-mode and M-mode for visualizing the tip of a needle as it was introduced via the hole in the transducer and penetrated the skin and deeper tissues. The tip of the needle was visible as a peak on the oscilloscope in A-mode or as a bright dot in M-mode. They used this technique for aspiration of fluid from the thoracic cavity, abdominal cavity, pericardium and renal cysts. In the same article they wrote: “Previously, most aspiration techniques were performed in a hit-or-miss fashion. With this new ultrasonic technique, however, the needle may be accurately guided into the area of interest, and changes of the fluid space during aspiration are known at all times.” Later developments, including the use of real-time B-mode have led to a wide repertoire of diagnostic and interventional procedures like ultrasound guided biopsies, installation of contrast media, different kinds of catheterizations, nephrostomy, cholecystostomy, gastrostomy, abscess drainage, introduction of central venous catheters, selective alcohol injections, radioactive therapy, laser, microwave therapy and cryosurgery [63].

7.3.1 Ultrasound and breast reconstruction with a DIEP flap

Hand-held Doppler is still an invaluable tool in the hands of general as well as vascular and plastic surgeons. In 1990 Taylor et al. reported on the use of hand-held Doppler in the planning of perforator flaps [64]. The use of this instrument has a distinct learning curve and it takes time to become proficient with the technique. Arteries and veins have their own characteristic Doppler sounds. In 2000 Giunta et al. published a study on the use of hand-held Doppler in the preoperative planning of 46 free perforator flaps including 32 DIEP flaps and 8 superior gluteal artery perforator (SGAP) flaps [65]. Prior to the operation, a hand-held Doppler was used to locate the acoustically loudest arterial Doppler sound at the donor site, which was marked on the skin together with other points giving arterial Doppler sounds. A coordinate system with the umbilicus as center was used to describe the locations where the arterial Doppler sounds were registered. Giunta compared these locations with the locations of perforators as they were observed intraoperatively. The authors found good correlation between pre- and intraoperative findings with an average distance of 8 mm between preoperative coordinates of the arterial Doppler sounds and intraoperative coordinates of the actual perforators. The instrument may be too sensitive and can detect perforators that are in fact too small to be used for perforator flap surgery [65-67].

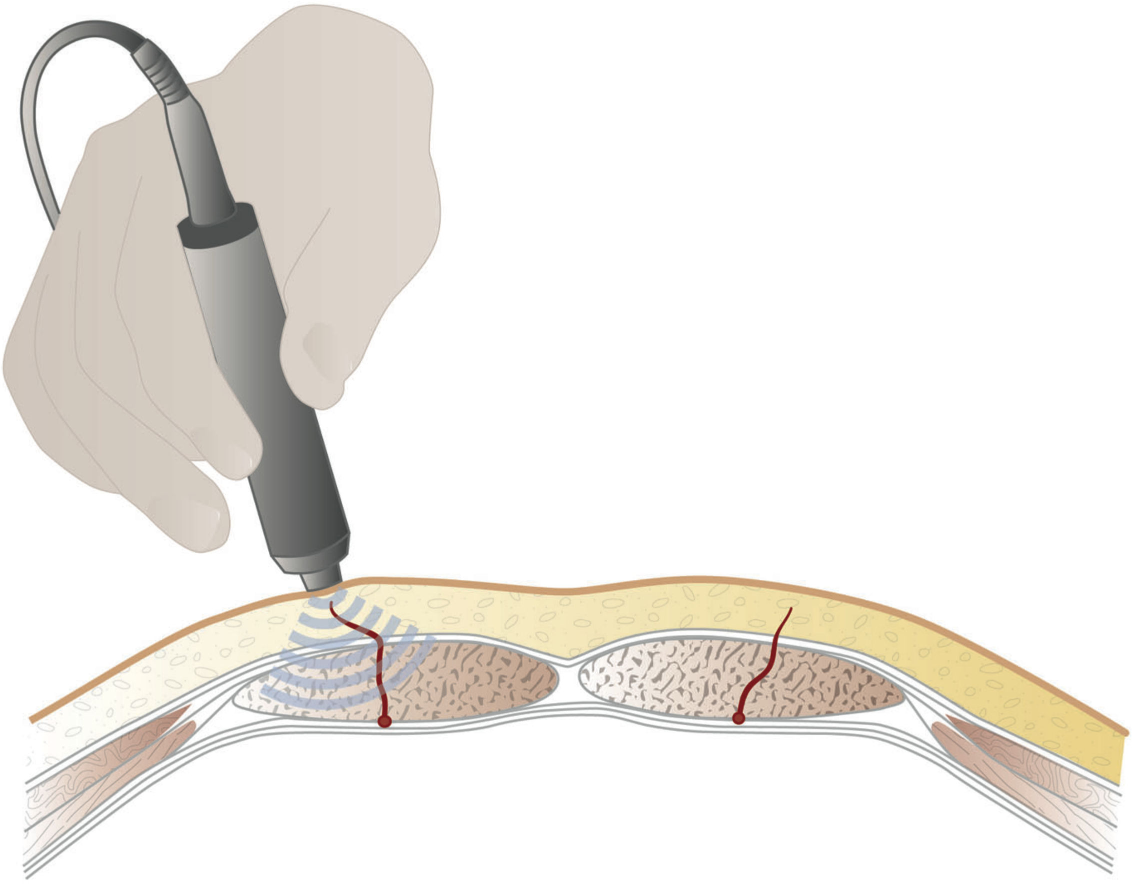

Figure 5 The hand-held Doppler transmits a continuous wave ultrasound signal. The frequency difference between transmitted and reflected ultrasound is sent to a loudspeaker. Hand-held Doppler is widely used for localizing abdominal perforators in DIEP breast reconstruction.

A weakness with the use of hand-held Doppler is the number of false positives, as not only perforators but also other arteries may give arterial Doppler sound [65, 67]. Blondeel et al. used hand-held Doppler in comparison with color Doppler and intraoperative findings in the planning of DIEP, SGAP and thoracodorsal artery perforator (TAP) flaps [67]. According to these authors, the hand-held Doppler is a handy and inexpensive tool to investigate the position and flow of superficial vessels. However, it does not distinguish perforating vessels from main axial vessels, and can create false positive localization of perforators if axial vessels run very superficially. On the other hand, color Doppler provides information on the three-dimensional course of the main axial vessels, their branches and the course of perforators. In addition color Doppler visualizes the structures through which the perforators run such as subcutaneous fat, muscles and fasciae. According to Blondeel, a drawback with color Doppler is cost as he estimates that a typical examination takes 45 to 60 minutes.

In 2010 Allessandro Cina et al. published an interesting study evaluating CTA versus color Doppler ultrasound in the planning of perforator flap surgery [45]. Their results showed an accuracy of 97 % for color Doppler and 91 % for CT angiography in identifying dominant perforator arteries. With color Doppler perforator arteries suitable for surgery were identified in 90 % of cases and in 95 % of cases with CT angiography. When comparing intraoperative findings with the results of preoperative imaging, color Doppler was superior in measuring the diameters of perforators. Interestingly, they found good agreement between the diameters measured as the sum of the perforating artery and vein with color Doppler and the presumed artery on CT angiography, indicating that CT angiography discriminates poorly between arterial and venous perforators. Even though CT was shown to be better at the evaluation of the intramuscular course of perforating vessels, it has lower spatial resolution than ultrasound. Due to the cost and radiation dose of CT angiography, Cina et al. recommend using color Doppler as first choice and supplying with CT when the results of color Doppler examination are inconclusive for surgery. In their experience, there was no significant difference between the mean times for examination and mapping of perforators with ultrasound (24 minutes) and CT (21 minutes).

7.4 Magnetic resonance imaging

The basis for magnetic resonance imaging (MRI) is the physical phenomenon called *nuclear magnetic resonance* (NMR) which was discovered before and developed just after World War II [68]. In 1971 Raymond Damadian reported in *Nature* that NMR could be used to detect malignant tissue [69], and a number of medical physicists started working to build a scanning device using NMR [70]. In 1973 Paul Lauterbur published a small article in *Nature*, initially rejected for publication, where he described what he called *NMR zeugmatography*, which actually was an early prototype of MRI [71].

In the 1970s practical use of MRI in medicine was still a distant dream. As late as December 1981 General Electric Company, which is now one of the leading manufacturers of MRI equipment, did not consider MRI technically feasible [72]. In 2003 Lauterbur and Mansfield were given the Nobel Prize in Physiology or Medicine for their work that made MRI possible. Damadian claimed that Lauterbur had stolen his idea about MRI, as he had filed a patent in 1972 where he considered the possibility of making T_1 measurements in vivo in the human body [72]. However, in his Nobel lecture, Lauterbur credited Damadian for discovering that some malignant tissue had longer NMR relaxation times than many normal tissues [73].

For the acquisition of MRI the body is placed in a strong magnetic field that is more than 10.000 times as strong as the magnetic field of the Earth. Short electromagnetic radio frequency (RF) pulses are sent into the body, where the energy is absorbed by hydrogen nuclei in the different tissues. These hydrogen nuclei, or protons, in turn transmit radio signals as echoes that can be picked up by a receiver coil. The strength of these echoes reflects the number of protons in different parts of the body.

To create images of specific organs of the body, the MRI scanner must acquire a signal from each part of these organs and effectively separate signals from different parts of the body. During a dinner in September 1971, Paul Lauterbur got the idea to use "a large set of simple linear gradients, oriented in many directions in turn in three dimensions" [73]. The theory of MRI was conceived. To accomplish this task, an MRI scanner uses separate gradient coils to vary the magnetic field with successive gradients in three dimensions. The signal picked up by the receiver coil is a sum of signals from every possible position in the body. By changing the magnetic gradients and adapting the right RF pulses, the scanner can make a huge data set and calculate the signal strength from all parts the chosen body region.

Signals from protons decay with unequal speeds depending on their various environments. Protons in different molecules have different magnetic properties, which influence the so-called relaxation time. Therefore the magnitude of the radio signal picked up by the receiver coil is monitored some time after the end of the transmitted RF pulse that started the process. Different tissues show different signal strengths, and hydrogen in different molecules may have different relaxation times. Hydrogen in pathological lesions and tumors often have other relaxation times than surrounding tissues which makes them detectable on MRI [68].

In 1984 Norwegian central authorities felt that the time had come to evaluate the introduction of MRI in Norway. The original intention of the authorities was to start with one unit at one of the university hospitals and gain some experience. However, the first diagnostic MRI unit in Norway was not purchased by the government but after private fund raising. This first MRI unit was installed at Stavanger County Hospital in 1986 [74]. In 1987 a government-appointed committee with the mandate of assigning healthcare priorities decided that MRI should have “zero priority” in the Norwegian health care system. MRI was defined as “health care services which are demanded, but unnecessary and without documented health effect”. The committee also claimed that MRI has “rather limited diagnostic value” and that its superiority in comparison to other modalities is restricted mainly to the diagnosis of rare conditions in the central nervous system [75]. Only university hospitals and the large regional hospitals were allowed to buy MRI equipment. These restrictions given by the government were not withdrawn until 1993 [76]. The Norwegian Professor of Radiology and MRI pioneer Hans Jørgen Smith stated in 2001, “the introduction of MRI in Norway is a good example of the inadequacy of central political control of detailed health political issues”. He did, however, see signs of change for the better in this country that he conclusively called “the last Soviet state” [74].

Today more than 10 years later things have changed. MRI has become standard equipment in almost all hospitals and all radiologists are supposed to learn basic MRI skills as an inevitable part of their radiological education. While the first prototypes needed several hours to produce an image, modern scanners produce images in seconds and even in real time during acquisition. New pulse sequences for different imaging tasks are continuously being developed for imaging of anatomy, pathology and dynamic processes like flow and drug metabolism. With functional MRI subtle changes in cerebral blood flow can be registered and linked to specific mental or physical activities. With MR spectroscopy we can get detailed information on the distribution of chemical substances in a defined region of interest within the body.

Unlike traditional X-ray examinations and CT, MRI does not use ionizing radiation. Except for the possibility of heating tissues by the RF pulses sent into the body, no potentially harmful side effects have been registered. Too much heating is avoided by limiting the amount of RF energy used by the different sequences. Normally a local tissue temperature increase up to 1 degree Celsius is accepted, and most imaging sequences cause much less heating [68]. The temperature effect is therefore no threat in the daily use of MRI. However, wire loops like ECG and other cables can act as RF antennas and cause overheating and even burns. Also jewelry and even some tattoos may act as antennas and cause local burns [68]. Unless the patient has a traditional pacemaker or other internal devices that are not MRI safe, such side effects can easily be omitted.

For many years it was a common conception that even contrast media used in relation to MRI examinations were totally safe. However, *nephrogenic systemic fibrosis* (NSF) is a seldom occurring but very serious complication of gadolinium based contrast media. The first cases of NSF were identified in 1997, but it took three years before it was reported in peer-reviewed literature, and its correlation with gadolinium based contrast media was not reported until 2006 [77]. Almost all documented cases of NSF have occurred in patients with moderate or severe renal dysfunction [78]. Today it is common practice to give gadolinium based contrast media only to patients without renal failure.

The good tissue contrast, high spatial resolution and to a large degree lack of harmful side effects have made MRI a very attractive alternative in a wide range of indications for medical imaging including plastic surgery. Most conditions that cause anatomical changes or tissue edema may be visualized with MRI.

7.4.1 MRI and breast reconstruction with a DIEP flap

CTA is by many considered the gold standard in preoperative perforator mapping in DIEP breast reconstruction, but due the inevitable exposure to ionizing radiation many have searched for an X-ray free alternative. Rozen et al. used both 1.5 and 3 Tesla MRI and compared their results to CTA [79]. In their experience both CTA and MRI angiography were able to identify the DIEA and its branching pattern in all cases. MRI was able to identify the location of some perforators with high accuracy, but was unable to identify all the perforators. CTA showed a greater capacity than MRI for visualizing the course of perforators in the subcutaneous, subfascial and intramuscular planes.

Higher spatial resolution is achievable with high field strength magnets. In 2008 Greenspun et al. reported on their use of 3 Tesla MRI angiography with a gadolinium based contrast medium for the preoperative mapping of perforators [80]. In their material abdominal wall perforators with a diameter of 1 mm could be reliably visualized. In 2009 Chernyak et al. also reported on the use of 3 Tesla MRI with gadolinium contrast [81]. Using intraoperative findings as gold standard, they reported that MRI was able to localize 97 % of the perforating arteries arising from the DIEA. The perforators visualized had an average diameter of 1.4 mm (range 1.0-1.6 mm).

Alonso-Burgos et al. published an article on their experience with 3 Tesla MRI and blood-pool contrast medium in the preoperative mapping of perforators in breast reconstruction [82]. Such a contrast medium stays intravascular for up to one hour after injection and does not rapidly diffuse into the interstitial space. Because the contrast medium stays within the blood vessels, it may improve the visualization of particularly distal vessels. According to their study, the use of blood-pool contrast medium effectively revealed the intramuscular course of vessels and the location of the main perforator vessels.

7.4.2 Some indications for MRI in plastic surgery

MRI is an important tool in breast imaging. It is the most sensitive method for detection of breast carcinomas invisible on ultrasound and mammography, and also an excellent method in the evaluation of silicone breast implant integrity [83]. In aesthetic plastic surgery MRI has been used in combination with a computer-assisted detection system to calculate the volume of breast implants with high accuracy [84]. The postoperative shape of round and anatomically shaped saline breast implants was studied with conventional radiography by Hamas in 1999 [20], and the shape of anatomically shaped silicone implants was evaluated with MRI by Nipshagen et al. in 2007 [85]. Nipshagen concluded that these implants largely maintain their shape postoperatively. However, patients were only examined in the supine position and the study said nothing about implant shape in other body positions.

MRI has been used to evaluate the survival of fat grafts for buttock contouring in cosmetic surgery [86]. Recently, MRI was also used in in a study evaluating a combination of vacuum treatment and autologous fat transplantation for breast augmentation [87]. In our own institution we have used MRI in the follow up of patients undergoing autologous fat transplantation to correct asymmetry after autologous breast reconstruction.

When it comes to the usefulness of MRI in plastic surgery, imagination and imaging are closely connected. Our imagination may be the most important limit to future applications of MRI.

7.5 Indocyanine green fluorescence angiography

Fluorescence is emission of light by molecules that has absorbed light or other electromagnetic radiation. The emission occurs at longer wavelengths than the exciting radiation, and the intensity of fluorescence is dependent on the intensity of the incident light [88]. This phenomenon has been known for centuries. In 1565, the Spanish physician Nicolás Monardes reported a peculiar blue color from an infusion of a certain wood from Mexico (*lignum nephriticum*) used to treat kidney and urinary diseases. This substance was expensive and Monardes recommended a test to reveal if the substance was real or a counterfeit. By mixing the substance with water, a bluish color would be seen if the substance was real. This is the first reported use of fluorescence in chemical analysis. Later fluorescence has been widely used in physics, chemistry, materials science and medicine [89].

In 1934 fluorescence angiography was introduced, and the first clinical studies with sodium fluorescein were performed in 1962 [90]. However, dye leakage through the capillary walls and a half-life time of 286 minutes have limited the potential clinical use of sodium fluorescein [91]. In 1956, the substance *indocyanine green* (ICG) received FDA approval for cardiovascular and liver function diagnostic purposes, and in 1975 ICG was granted approval for ophthalmic angiography [92]. Later ICG has been used in the evaluation of blood circulation in skin, determination of burn depths and the assessment of perfusion in skin flaps and cases of compromised wound healing [90].

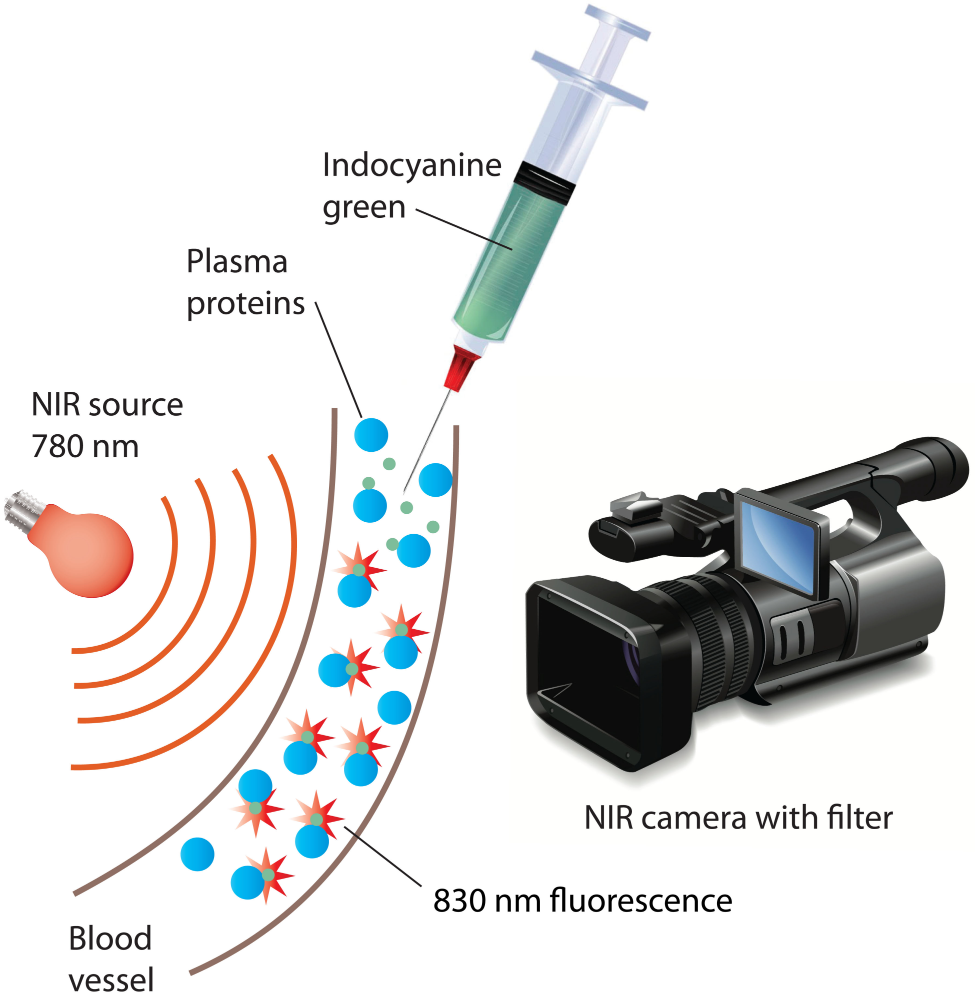

Fig. 6. ICG is injected intravenously and a 780 nm NIR source illuminates the tissues. ICG bound to plasma proteins emits NIR at 830 nm is captured by a video camera. A filter at the camera lens removes light with wavelengths below 830 nm.

In serum, ICG has its absorption maximum at 805 nm and a fluorescence emission maximum at a wavelength around 830 nm. These wavelengths are within the near infrared (NIR) spectrum, which is invisible to the human eye. Human tissue is relatively transparent to such radiation, which makes ICG fluorescence a valuable tool in the evaluation of subcutaneous blood circulation. ICG binds strongly to plasma globulins, limiting the washout time for the dye. Clinical and experimental studies have shown good correlation between the distribution of ICG and viability of skin tissue [93, 94]. Therefore, ICG fluorescence angiography (ICG FA) has been successfully used in plastic and reconstructive surgery to assess blood circulation in flaps and damaged tissue.

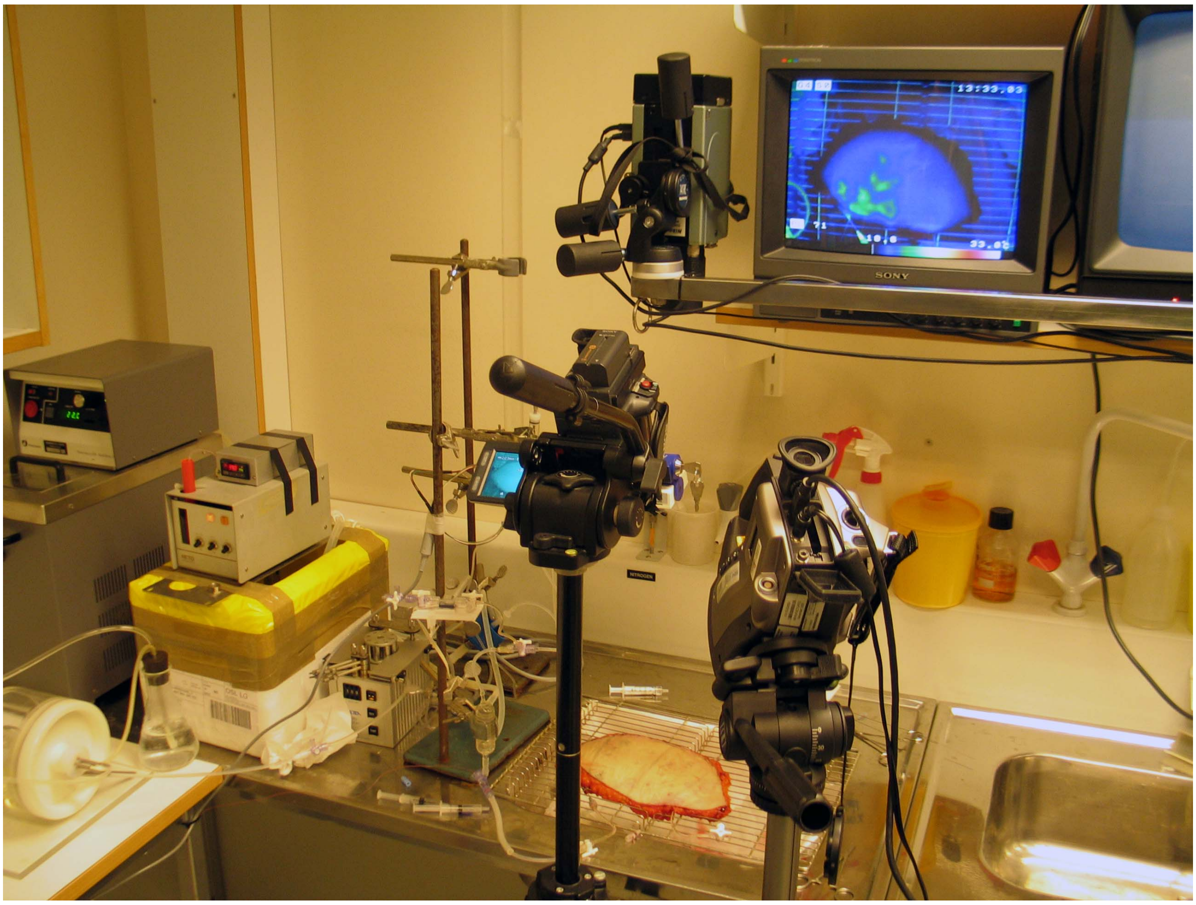

Figure 7 As described in paper I, isolated abdominal flaps, harvested from women undergoing abdominoplasty, were cannulated and perfused with oxygenated buffer. ICG was injected in selected perforators for fluorescence angiography. Warm and cold fluid was injected in the same vessel and the flap was monitored with an infrared camera.

After intravenous administration of ICG, the skin is illuminated with a monochrome NIR illuminator with a wavelength in the area around 780 nm. Charge-coupled device (CCD) and complementary metal-oxide-semiconductor (CMOS) sensors used in common video cameras are highly sensitive to NIR, a phenomenon that can be utilized to register fluorescence from ICG around 830 nm. Regular consumer video cameras are equipped with an NIR filter to prevent NIR light to reach the sensor, as this may cause interference to the image. However, many cameras have the option of bypassing this filter for night vision recording. Usually a small NIR emitting light emitting diode (LED) is used for illumination in night vision mode. By disabling the LED and using another filter that prevent visible light and NIR below 830 nm from reaching the sensor, the camera may register almost *only* NIR fluorescence from ICG (Fig. 6).

An important drawback of ICG FA is the need for intravenous injection of dye. In addition, the examination should be performed in darkness in order to minimize interference from other light sources. Sunlight and electric light sources are not limited to the visible spectrum, but they do also contribute with radiation in the NIR part of the spectrum.

A recent publication by Kikuchi et al. reports on the successful use a NIR fluorescence venography system in the pre- and intraoperative phase of varicose vein surgery called *Photodynamic eye* [95]. Within seconds after ICG injection, real-time images of varicose veins are easily obtained. According to Kikuchi the depth for visualization is limited to approximately 2 cm. In obese patients this obstacle could often be overcome by compressing the subcutaneous tissue or first performing a skin and superficial fascia incision prior to the injection of ICG.

Matsui et al. have developed an intraoperative imaging system that simultaneously displays surgical anatomy and NIR fluorescence from ICG for use in perforator flap design [96]. In addition to the NIR illuminator producing monochrome NIR light to excite ICG, their equipment also includes LEDs providing white light with wavelength within 400-650 nm. The system has two cameras, one NIR sensitive camera with a filter that removes visible light as well as the NIR radiation from the NIR illuminator and one regular video camera that captures color video illuminated by the white light LEDs. Images from the two cameras are merged and displayed at a common display, providing the surgeon with information about both anatomy and fluorescence from ICG in the underlying vessels.

7.5.1 ICG FA used in plastic surgery

Thermal injuries are treated by plastic surgeons. The depth of the wound must be evaluated when evaluating the need for surgical excision and skin grafting. Deep dermal wounds and so-called full thickness burns require surgical treatment. This is a difficult clinical evaluation and ICG FA has been used as an effective tool in the evaluation of skin perfusion after thermal injuries [97]. ICG FA offers a dynamic visualization of vessel patency in the injured skin in real time with high accuracy [98] and the findings of ICG FA have been shown to correlate with histology and clinical outcome of patients with burns [99].

Evaluation of tissue circulation is also very important in trauma surgery and microsurgery performed by plastic surgeons. Traditionally this evaluation has been based on subjective evaluation of tissue color, capillary reperfusion and temperature. ICG FA effectively visualizes tissue perfusion with a significantly higher prognostic value than traditional clinical evaluation [90, 100].

7.5.2 ICG FA and breast reconstruction with a DIEP flap

ICG FA is a valuable tool in the evaluation of flap perfusion. In a study published in 2002 Holm et al. used ICG FA in 15 patients undergoing pedicled skin-flap surgery. In their experience, ICG FA was highly sensitive at detecting regionally decreased blood flow of pedicled flaps [101]. In 2010 Francisco et al. reported on ICG FA in breast reconstruction with a DIEP flap [102]. They wrote that ICG FA provides information in real-time on the position of abdominal wall perforators, patency of anastomoses and information about areas within the flap that have poor perfusion and therefore should be discarded during the operation. In 2012 Losken et al. reported on the use of ICG FA in 77 pedicled TRAM flaps, 22 muscle-sparing free TRAM flaps and 37 DIEP flaps [103]. Their study showed that lower abdominal free flaps such as the DIEP flap have better perfusion than pedicled TRAM flaps.

As we will see in the next section, ICG fluorescence angiography may be replaced by simpler and non-invasive techniques such as thermography for certain indications. However, with emerging new technology including CCD or CMOS sensors with higher sensitivity and high-definition video resolution, we may expect better visualization of blood circulation in small vessels and perhaps also the ability to visualize circulation at deeper levels in the subcutaneous tissues. ICG fluorescence angiography certainly has a place also in future diagnostics and research.

7.6 Infrared thermography

Human body temperature has been used to diagnose disease since ancient times. Hippocrates (460-370 B.C.) applied wet mud to the skin and observed faster drying over a tumor compared to normal tissue. This is the first recorded experiment showing that pathology in the body may be visualized by distinguishing between skin areas with different temperatures. However, measuring temperature was a subjective skill for two millennia until Santorio Sanctorius developed the first thermometer in 1611. He used his new invention to demonstrate different core temperatures of humans in health and disease. The clinical thermometer with a limited scale around 37 degrees Celsius was developed by Dr. Carl Wunderlich in 1868. During the first half of the 20th century, daily body temperature measurement was implemented as a hospital routine [104].

As illustrated by the experiment by Hippocrates, there are also situations were knowledge of the temperature *distribution* over an area of the body can give valuable information about the patient's condition or disease. This information can be displayed as a *thermogram,* which visualizes the temperature of every spot in a certain region of interest [105]. The word thermogram was first used by John Herschel (1792-1871) who focused solar radiation with a lens on a suspension of carbon particles and alcohol to make an image. His father William Herschel had shown that heat behaves like light and demonstrated with a prism that the heat could be measured with a thermometer in the dark area below red light at the end of the visible spectrum. This part of the electromagnetic spectrum is called infrared radiation.

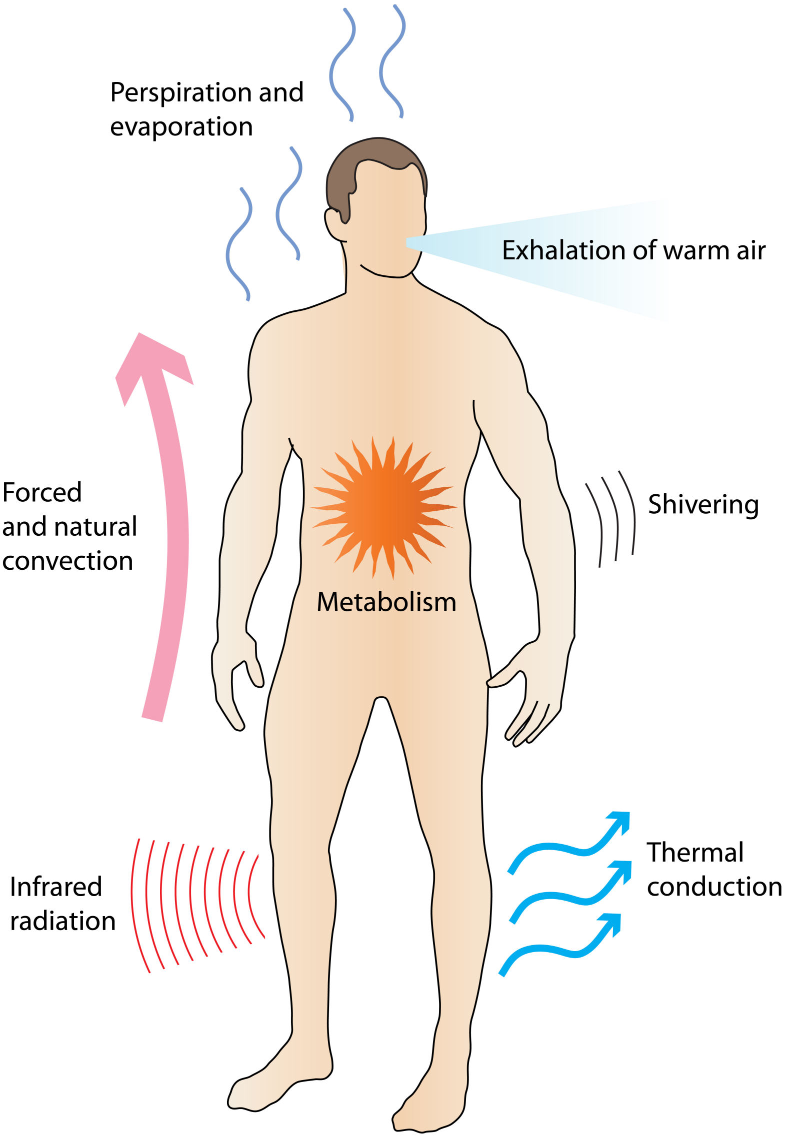

Figure 8 The body keeps a constant temperature by balancing heat production and heat loss. Heat is produced by metabolism and muscle activity. Mechanisms of heat loss are conduction, convection, evaporation and radiation.

After World War II equipment was developed to detect infrared radiation for military purposes. The technology is widely used for border surveillance, law enforcement, ship collision avoidance, guidance systems, heat seeking missiles and night vision equipment [106]. The first medical infrared images were made in 1959. These images had very low resolution and it took several minutes to produce one image. However, this was a large step forward as doctors could see radiation in the invisible infrared spectrum from the patients.

Humans are homeotherms, which means that we are capable of maintaining a constant temperature that is different from that of the surroundings [107]. There is a fine balance between heat production and heat loss. Muscle contraction and metabolism produce heat, while the blood is transporting heat through the body. Heat loss is possible through conduction, convection, evaporation and radiation (Figure 8) [108]. However, at an ambient temperature between 18 and 25 degrees Celsius, the most important mechanism of heat loss is infrared radiation.

A body's thermal emittance ($W/m^2/\mu m$) is a function of both temperature and emissivity, where emissivity (**Є**) is an index value from 0-1 describing the ability of a surface to emit energy via radiation relative to a perfect black body radiator [109]. The human body has an emissivity index of approximately 0.98, which is very close to 1.0 of a perfect black body radiator. This implicates that it behaves almost as a perfect black body in relation to infrared radiation. A black body at a constant temperature emits electromagnetic radiation according to *Planck's law,* which means that the frequency spectrum of the radiation is determined by temperature alone. Therefore, an infrared camera can easily be calibrated to measure absolute surface temperatures of the human body with high accuracy [110].

It is known that many tumors have increased blood circulation and are hotter than normal tissues, and with the introduction of infrared technology in medicine, many hoped that this could reveal cancer in the body. In 1956 Ray Lawson published an article where he had used a so called Baird Evapograph to create a thermogram showing that the skin temperature was increased over a malignant breast tumor [111]. In the same article, he wrote that "it is fascinating to speculate on the diagnostic possibilities of a heat-sensitive imaging device capable of surveying breasts in much the same manner as mass screening by chest radiography is carried out for the early detection of tuberculosis". Following the development of more sensitive infrared imaging devices, many centers started using infrared thermography in their search for breast cancer. However, in 1977 Feig et al. published a review of studies including a total of 16.000 women showing that even though large tumors were visible on thermography, only 21 % of tumors between 0.5 and 1 cm were visible with this method [112]. Some centers still use thermography as a supplement to other diagnostic methods, but after the publication from Feig et al. the interest for thermography in cancer screening has been considerably reduced.

Studies have shown that there is a good correlation between skin perfusion and skin temperature. Measurement of skin temperature can therefore provide indirect information about skin perfusion [113-115]. Not only cancers but also many other pathological conditions cause increased skin temperature. Therefore medical thermography has been used in fields like neurology, rheumatology, dermatology, oncology and different types of surgery [47, 116]. Today the technique is also widely used in research. A search in PubMed with the term “thermography” gives a search result of almost 7.000 papers.

Following the rapid development of infrared technology used for military and industrial purposes, more advanced and less costly equipment has become available for medical use. Lightweight, solid state, focal plane array (FPA) micro bolometer sensor cameras are now available. These cameras have no need for cryogenic sensor cooling and are easily transportable [106]. Such cameras are highly affordable in comparison to other medical imaging equipment. Modern infrared cameras also come with advanced image processing software for real time imaging and image analysis.

In static infrared thermography, single images are taken without exposure of the area of interest to a thermal challenge prior to image acquisition. The use of static infrared thermography in clinical practice is based on the assumption that there exists a basically symmetric distribution of body surface temperature between the right and left side. The interpretation of static thermograms mainly depends on the identification of asymmetric temperature distribution.

However, due to complex vascular patterns one cannot always rely on asymmetry as an indicator of disease. By monitoring skin temperature after a thermal challenge, dynamic information on skin circulation can be obtained. This technique is called *dynamic* infrared thermography, or DIRT. The temperature challenge, which consists of either cooling or heating, may be achieved with fan cooling, water immersion, application of a steel plate on the skin or any other technique that provides a uniformly distributed temperature change to the tissues.

7.6.1 DIRT and breast reconstruction with a DIEP flap

In 1986 Theuvenet et al. published an article on what they called *thermographic assessment of perforating arteries* [117]. Although using another name, this was actually the first reported mapping of perforators with the use of DIRT in the literature. The authors had experienced failure in using hand-held Doppler for preoperative perforator mapping in high-risk patients with poor skin perfusion. They cooled the skin and temporarily interrupted the arterial blood flow of the lower extremity with an inflatable cuff. After deflating the cuff emerging hot spots were registered with an infrared camera. Although not performing DIEP flap surgery, their pioneering work on DIRT laid the foundation for later use of DIRT in DIEP flap surgery. Theuvenet et al. reported that perforating arteries could be located in a non-invasive accurate way with their technique.

Itoh and Aray described the use of DIRT in perforator mapping in DIEP breast reconstruction in 1993 [118]. In 1995 Salmi et al. used thermography to study hot spots corresponding with perforators in free TRAM breast reconstructions [119]. They concluded that thermography is a potential method for mapping cutaneous perforators pre-, intra- and postoperatively and for monitoring flaps bedside. Arterial perforators that transport blood towards the skin cause a local heating of the skin surface that can be visualized as hot spots on infrared images.

In our institution DIRT has been used in the preoperative mapping of perforators for almost a decade, and in 2005 a dedicated laboratory for medical thermography in the Department of Radiology was established. Hippocrates smeared “dirt” on the patient’s skin to visualize higher temperature over a tumor. Now we use DIRT with analysis of the rate and pattern of rewarming or cooling after at thermal challenge towards a thermal equilibrium to obtain indirect information on skin perfusion. As more research is done and new scientific documentation is provided, medical thermography has the potential of becoming a widely used imaging modality and a natural part of daily radiological practice.

8. Papers included in the thesis

Four papers are included in this thesis. The first three deal with the use of infrared imaging in the evaluation of skin perfusion and mapping of abdominal wall perforators in the planning of reconstructive plastic surgery, while the fourth is about the use of MRI in studying the properties of anatomically shaped silicone implants used in breast augmentation and reconstruction. The purpose of the first three studies was to evaluate the use of DIRT as an imaging technique for perforator mapping in breast reconstruction with a DIEP flap. The purpose of the fourth study was to evaluate the form stability of the Style 410 anatomically shaped cohesive silicone gel-filled breast implant using MRI. A wide range of imaging techniques is used in these studies, and the common denominator is how imaging can contribute to answer questions posed by the plastic surgeon. While the fist paper describes an experimental study where isolated abdominal flaps are studied in vitro in a university laboratory, the other three are all clinical studies performed in a hospital environment.

Infrared thermography has been used in medicine for several decades. However, the use of DIRT for perforator mapping in plastic surgery was first reported in 1986 by Theuvenet [117]. The technique has not gained widespread acceptance within plastic surgery. To explore the possibilities and limitations of DIRT as an imaging method for perforator mapping, our research group has performed several studies on DIRT of which three are included in this thesis. The fourth study in the thesis does not introduce a new imaging technique, but MRI is used in a novel way to visualize the behavior of breast implants in vivo as the body position is changed from supine to prone.

All four studies illustrate the value of collaboration between different disciplines. The three first studies were performed to evaluate DIRT as an imaging method for perforator mapping while the last implements the well-known modality MRI to answer questions that would otherwise be difficult to answer from the plastic surgeon's clinical point of view.

Paper I: Visualising skin perfusion in isolated human abdominal skin flaps using dynamic infrared thermography and indocyanine green fluorescence video angiography

Reconstructive surgery may restore form and function after traumas, surgical treatment of pressure sores, cancer and congenital defects by moving tissue from one part of the body to another. However, such tissue transfer is not possible unless the transferred tissue has adequate blood perfusion. Sir Harold Delf Gillies (1882-1960), who has also been called the father of plastic surgery, spoke of plastic and reconstructive surgery as a constant struggle between beauty and blood supply [120].

In perforator flap surgery large flaps rely for their blood supply on a tiny perforator with a diameter that may be less than a millimeter. The consequences of flap failure are dramatic to the patient and cause huge costs to the health care system. With such marginal vessel capacity, the battle for blood supply becomes even fiercer. The surgeon must choose a suitable perforator that is capable to provide adequate perfusion to the flap to avoid partial or total flap failure. Monitoring flap perfusion during and after the operation is also important to discover inadequate perfusion or perfusion failure as early as possible.

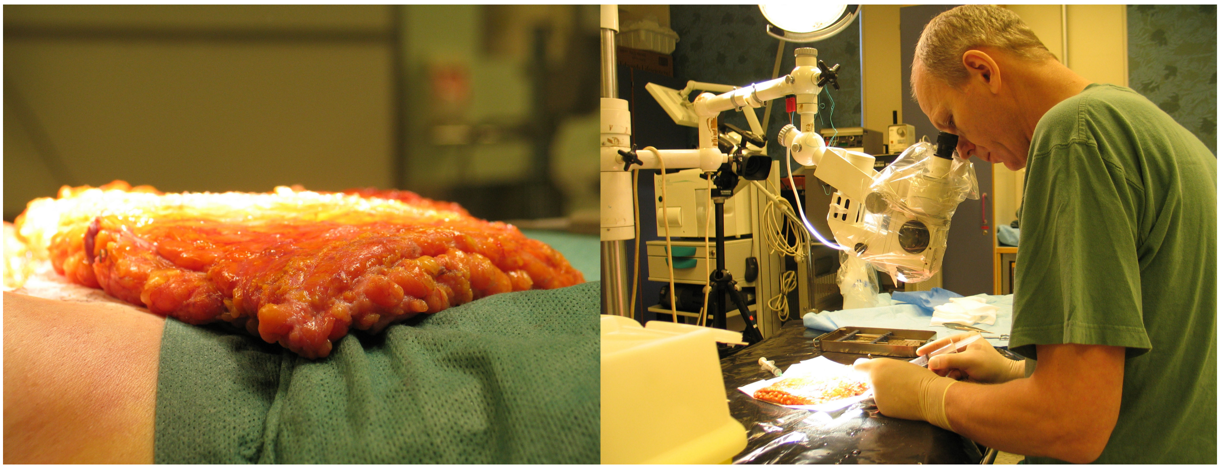

Figure 9 Abdominal flap harvested by abdominoplasty and perforators cannulated with microsurgical technique.

The aim of the study reported in paper I was to investigate whether the use of DIRT in an isolated human skin flap can provide information on free perforator flap perfusion that is comparable to the information obtained with ICG FA. ICG FA is an established method that is able to visualize circulation in the skin and subcutaneous vessels. As described before, the technique has a definite place in evaluating perfusion in flap surgery. The method has shown to be a reliable imaging technique to monitor flap perfusion. However the drawbacks are evident. Intravenous injection of ICG is necessary and, although seldom occurring, allergic reactions to ICG are possible. The examination should be performed in complete or partial darkness. Fluorescence is only visible for a limited period of time after injection of ICG due to its short half-life. DIRT on the other hand is a simple method that does not require injections, the examination can be performed in daylight and may be repeated as many times as the surgeon wants.

Figure 10 The cannulated perforator examined with DIRT and ICG FA.

In the experimental study of paper I isolated abdominal flaps harvested from women undergoing abdominoplasty were used. These flaps were artificially perfused with oxygenated buffer solution in the laboratory. Individual perforator arteries from the DIEA were cannulated. In some flaps, the SIEA, SIEV and superficial circumflex iliac artery (SCIA) were cannulated. The vessels were perfused with warm and cold fluid while the flaps were continually monitored with in infrared camera.

The same vessels were also perfused with ICG and monitored with ICG FA. A total of 19 selected vessels in 8 flaps were examined with both methods. Qualitative assessment of the perfusion patterns from DIRT and ICG FA showed a good correspondence between the extent of the perfused areas visualized with DIRT and ICG FA.

At the end of the experiment all 8 flaps were perfused with iodinated contrast medium and examined with conventional radiography. The vessels and the perfused area with the contrast medium visualized on the radiographic images corresponded well with the vessels and perfused areas visualized with DIRT and ICG FA. Although not described in the published article, we also performed CTA of all 8 flaps after the experiment visualizing the same vessels as conventional radiography with CTA. Three-dimensional reconstructions of the CTA images graphically visualized the perforator vessels in their course through the abdominal flap (Figure 11).

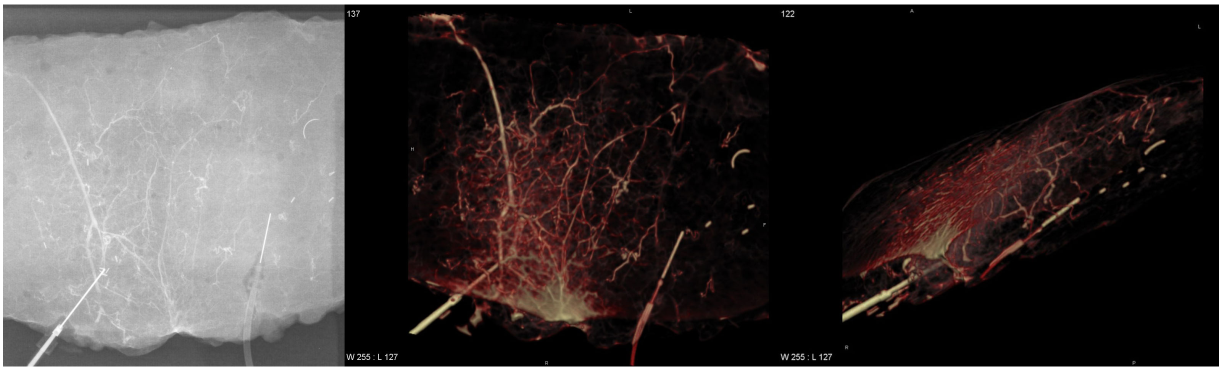

Figure 11 Iodinated contrast medium was injected in a perforator prior to conventional X-ray (left) and CTA examination of the flap (middle and right).

This study provided useful documentation based on an experimental laboratory setup isolated from possible sources of errors in a clinical setting. By using isolated abdominal flaps the results were not influenced by factors such as changes in the patient's blood pressure or changes in blood circulation caused by other vessels in the abdominal area.

In this in vitro setting it was possible to cannulate several different vessels in the same flap and to perform several subsequent experiments with the same flap. This setup also allowed for repeating the experiments several times to evaluate if the results were consistent when the experiments were repeated. Selective cannulation and perfusion of perforators could also be done during perforator flap surgery, but the risk of damaging the flap's circulation during the procedure would certainly have limited the experiment and not allowed for several cannulations and perfusions in the same way as in the laboratory setting.

A limitation of this study is that the results not necessarily can be directly transferred to a clinical setting. However, the study showed that the non-invasive method DIRT provides information on tissue circulation that is comparable to the information obtained with the invasive technique ICG FA. The studies reported in paper II and III were performed to see if the results of this experimental study are transferable to daily practice in perforator flap surgery.

Paper II: The value of dynamic infrared thermography (DIRT) in perforator selection and planning of free DIEP flaps

The aim of this prospective clinical study was to investigate whether preoperative use of DIRT contributes to the selection of a suitable perforator and to the planning of free DIEP flaps in autologous breast reconstruction.

In this study 27 women participated, all undergoing autologous breast reconstruction, of whom 23 with a DIEP and 4 with a superficial inferior epigastric artery (SIEA) flap, participated in the study. Preoperatively, all women were examined with hand-held Doppler and DIRT. Hand-held Doppler was used to localize arterial Doppler sounds, which were marked on the skin. The exposed abdomen was subjected to 5 minutes acclimatization at room temperature before a cold challenge was delivered by blowing air at room temperature with a desktop fan for 2 minutes. After 3 minutes recovery and with the infrared camera running, emerging hot spots on the infrared images were localized on the abdominal skin and these spots were examined with hand-held Doppler. If arterial Doppler sound was present, its location was marked with a cross on the skin.

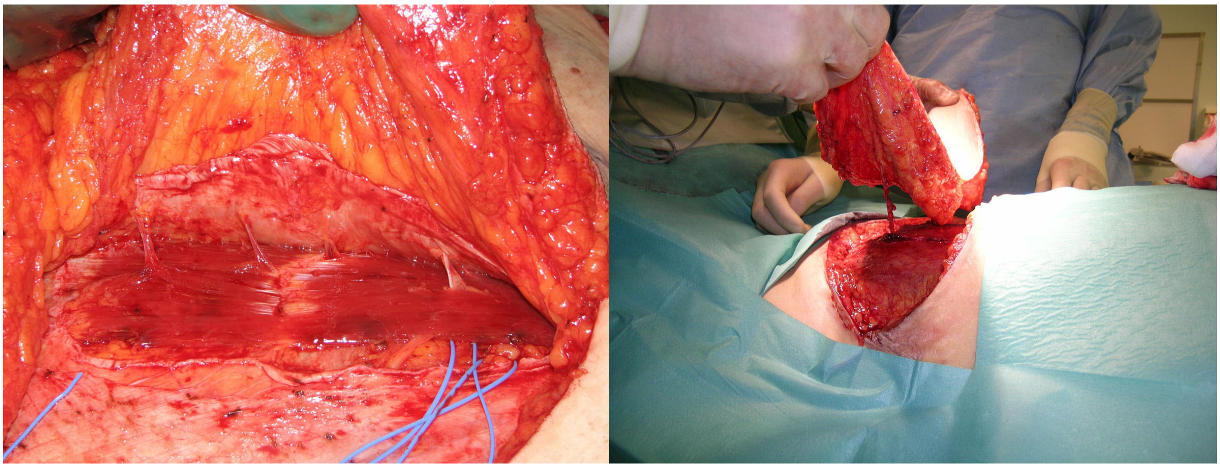

Figure 12 Left: Perforators from the DIEA and DIEV coming through the rectus abdominis muscle towards the skin and subcutaneous tissue. Right: The DIEP flap receives its blood supply through one of these perforators.

A perforator was selected on the following criteria:

1. A rapidly appearing hot spot after the cold challenge
2. The hot spot was associated with arterial Doppler sound
3. The perforator was not located at the edge of the flap

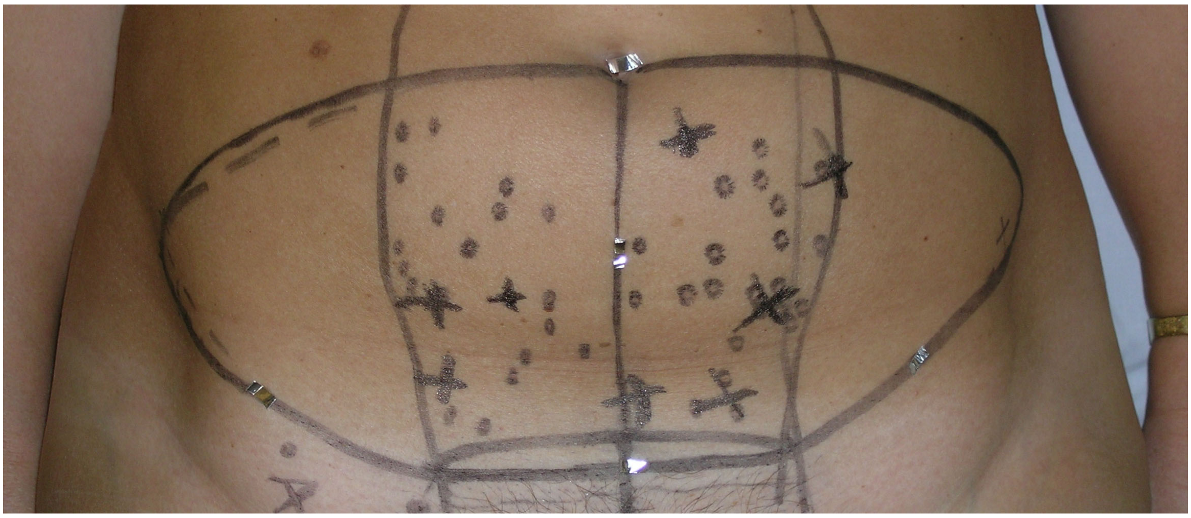

Figure 13 Hot spots associated with arterial Doppler sounds marked with crosses.

All hot spots with a rapid rewarming were also associated with arterial Doppler sounds. A positive correlation was observed between the brightness of the hot spots and the volume of the audible Doppler signals. Intraoperatively, a suitable perforator was always found in the area corresponding with the selected hot spot on the abdominal wall. All DIEP flaps were based on the perforator that was associated with the selected hot spot. All flaps survived, although 3 patients suffered minor partial flap loss. However, the loss was not large in these cases and all patients had enough viable flap tissue to obtain a good postoperative result.

In 8 of these patients, an additional preoperative CTA examination of the abdominal wall was performed. The localization and size of the different perforators visualized with CTA were compared with the findings from hand-held Doppler and DIRT. All selected hot spots could be related to a clearly visible perforator on CTA. To our knowledge, this was the first comparison of clinical DIRT and CTA reported in the literature.

Figure 14 At the University Hospital North Norway a dedicated thermography laboratory is established within the Department of Radiology. A high quality infrared camera is less expensive than most other equipment used for diagnostic imaging.

The results from the study in paper II show that DIRT may provide reliable qualitative information on the position and capacity of perforators without the use of ionizing radiation or intravenous contrast injection. DIRT demands less expensive equipment than CTA, the examination is not difficult to perform and the results are easy to interpret.

Paper III: Perforator mapping in breast reconstruction: A comparative study of dynamic infrared thermography (DIRT), computed tomographic angiography (CTA) and hand-held Doppler

In the 3rd paper the aim of the study was to investigate how the results of DIRT in the preoperative planning of DIEP flaps for autologous breast reconstruction relate to the findings of CTA and hand-held Doppler. 25 patients scheduled for breast reconstruction with a DIEP flap participated in this prospective clinical study.

In the same way as reported in paper II, all patients were examined with both hand-held Doppler and DIRT preoperatively. A suitable perforator for DIEP breast reconstruction was selected on the same criteria in this study as in paper II. The selected perforator had to be associated with a rapidly appearing hot spot after the cold challenge, this location had to be associated with arterial Doppler sound, and the perforator could not have its location near the edge of the flap.

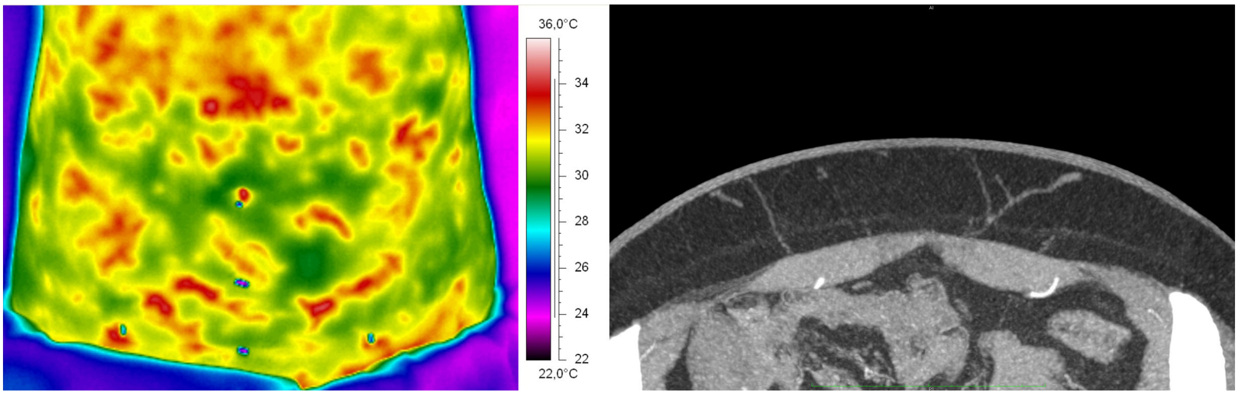

Figure 15 Hot spots on DIRT (left) associated with perforators visible on CTA (right).

To describe the locations of perforators and hot spots, we made a quadrant system in which the flap surface overlying the fascia of each rectus abdominis muscle was divided into four quadrants (Figure 16). Other authors have used a coordinate system to describe the location of perforators in relation to the umbilicus. However, we have noticed that the distance between the exit point of each perforator through the fascia and its associated hot spot decreased as soon as the skin incisions were made. Following skin contraction, the hot spots usually moved more medially and became positioned closer to the perforators' fascial exit points. As absolute coordinate values for hot spots will not be identical pre- and intraoperatively, we suggest that the use of a quadrant system as it is more valuable to the surgeon than using an absolute coordinate system.

Our results showed that the first appearing hot spots on DIRT images always were associated with clearly visible perforators on CTA. These hot spots were also associated with arterial Doppler sounds. The study showed that analyzes of the rate and pattern of rewarming of hot spots on DIRT provided valuable information for perforator selection in DIEP breast reconstruction. In addition to information about localization of perforators, DIRT also provides information on the perforator's hemodynamics. A rapid rewarming at the hot spot indicates that the associated perforator transports more blood to the skin surface than a perforator that produces slower rewarming. A progressive rewarming indicates a well-developed vascular network around the hot spot. By observing the hemodynamics on DIRT one may select a perforator that not only has large blood flow but also a well-developed vascular network in the flap.

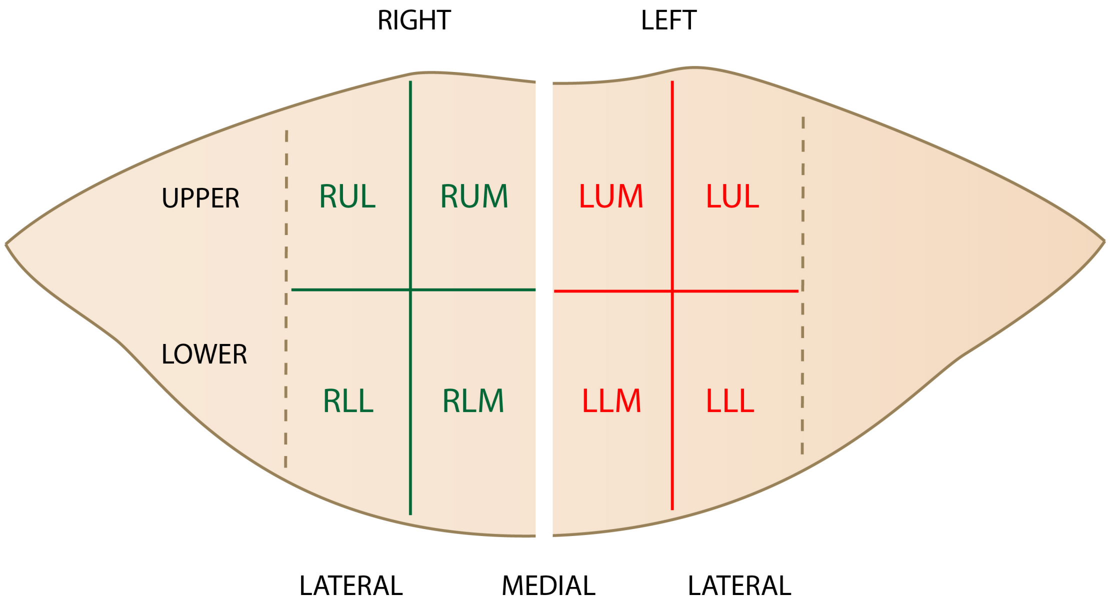

Figure 16 To describe the localization of hot spots the area over each rectus abdominis fascia is divided into four quadrants.

In a number of cases large periumbilical perforators were seen on CTA, but not all of these were associated with bright hot spots. This finding indicates that these perforators do not transport much blood (and therefore heat) to the skin surface. We postulate that such perforators consist of a large vein and a small artery, and that the large vein communicates with the SIEV. Both intraoperative findings and the CTA images support this postulation (Figure 17).

The main object of this study was to relate the DIRT findings to findings on CTA, the considered gold standard for perforator mapping. Our study showed that bright hot spots on DIRT always corresponded to visible perforators on CTA. However, not all visible perforators on CTA were associated with hot spots on DIRT. Unlike CTA, DIRT provides real time qualitative information on the hemodynamic properties of perforators. The quadrant system introduced in this paper defines a limited anatomical area in which the surgeon needs to do meticulous dissection to localize a suitable perforator intraoperatively. The surgical outcome of the breast reconstructions showed that all flaps survived on the perforators selected from the DIRT examination. Based on the results from the study in paper III it is concluded that DIRT can replace CTA in preoperative perforator mapping.

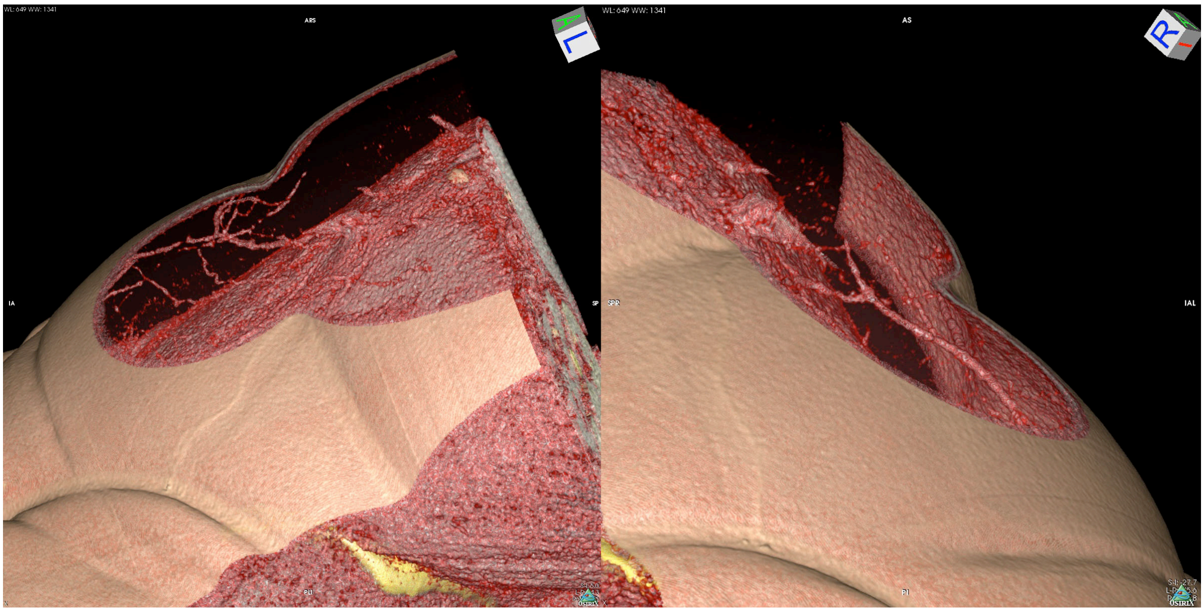

Figure 17 3D reconstructions showing periumbilical perforators that communicate with the SIEV on both sides of the abdomen. These perforators were not associated with bright hot spots on DIRT.

Paper IV: Form stability of the Style 410 anatomically shaped cohesive silicone gel–filled breast implant in subglandular breast augmentation evaluated with magnetic resonance imaging

Breast implants are used in breast augmentation surgery as well as in reconstructive surgery after breast cancer treatment. Among cosmetic operations, breast augmentation is one of the most frequently performed procedures. For breast cancer patients who do not want a complex reconstructive procedure with autologous tissue, reconstruction with an implant can be a good alternative.

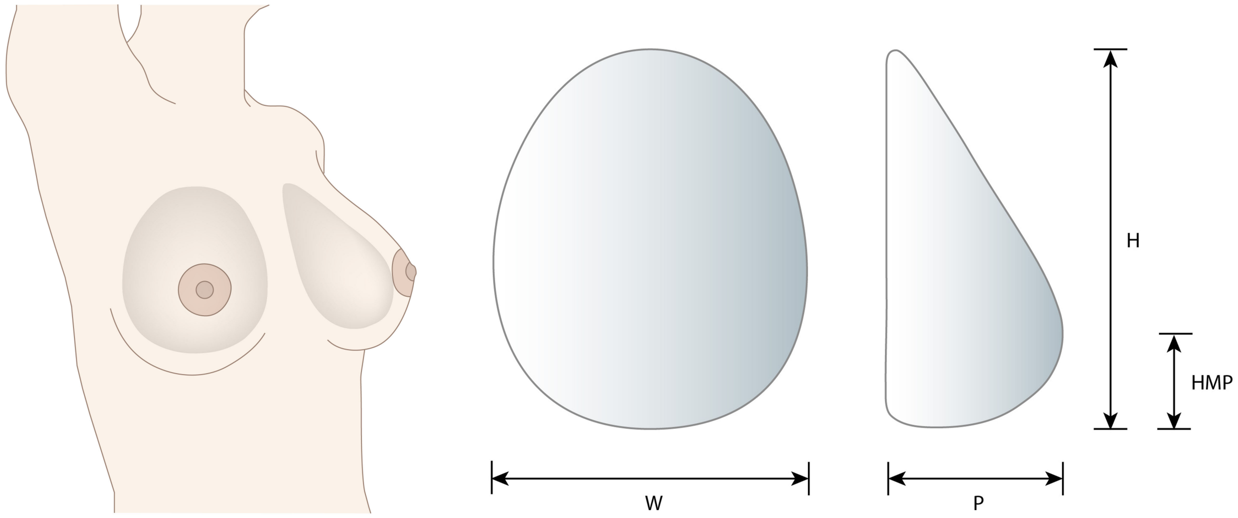

Figure 18 Anatomically shaped breast implants and their measurements in the coronal and sagittal planes. W= width, P = projection, H = height, HMP = height of maximal projection.

Since the introduction of silicone breast implants in 1963, several new generations of implants have been developed. The so-called anatomically shaped cohesive silicone gel-filled implants were developed to overcome several drawbacks associated with former implant generations. The cohesive silicone gel has a higher viscosity than the silicone gel traditionally used in breast implants. This is believed to reduce the frequency of implant rupture, silicone leakage and migration to regional lymph nodes. The anatomical shape is claimed to result in increased lower pole fullness of the breasts, giving them a more natural shape than the traditional round implants [8-10].

Cohesive gel implants have been marketed as “form-stable”, although this term has never been accurately defined in the literature. Critics have claimed that the increased viscosity reduces the implant’s ability to behave naturally after implantation and have given these implants the nickname “gummy bear implants”. In their core study on the Style 410 implant published in 2007 Bengtson et al. defined a form-stable implant as an implant that will maintain its dimensions and form in any position [11]. Several studies report good aesthetic results with anatomically shaped implants [121, 122]. However, most studies are based on patient satisfaction and the surgeon’s subjective evaluation of the postoperative results.

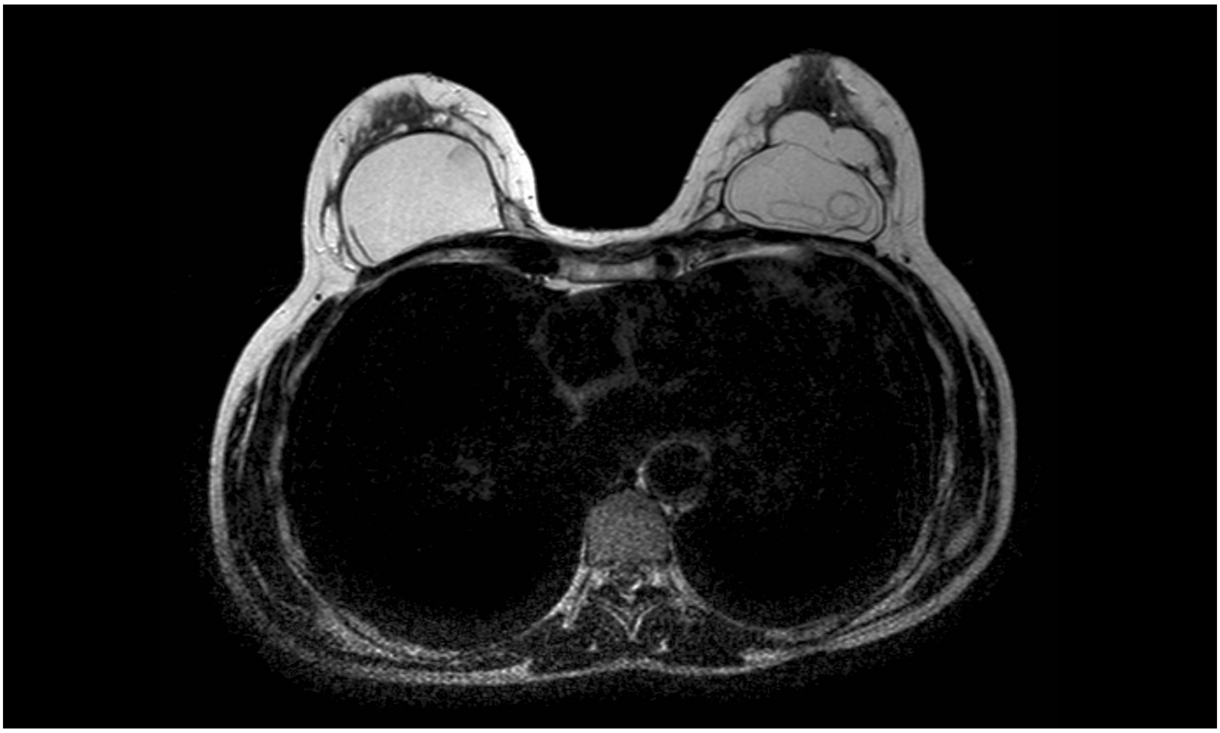

Figure 19 MRI showing intra- and extracapsular rupture of traditional round soft silicone gel-filled breast implants.

Exact knowledge about the behavior of such breast implants after implantation has been lacking. The Style 410 breast implant is frequently used in cosmetic and reconstructive surgery. This implant has been advertised as a form-stable breast implant. Our study was designed to evaluate whether the dimensions and form of the Style 410 implant are influenced by body posture. MRI is an established imaging method for the evaluation of breast tissue and the integrity or possible rupture of silicone implants. Other authors have studied the static dimensions of such implants in the supine position [85]. By studying the implant dimensions in both the prone and supine body positions, it is possible to evaluate a possible effect body posture may have on the dimensions of the breast implant. Such knowledge will help the surgeon to inform the patient more precisely on the possible postoperative result.

A total of 9 healthy women participated in this study. They had all undergone breast augmentation with the same type cohesive anatomically shaped silicone implants Style 410 produced by Allergan. All 18 implants were implanted via an inframammary incision and placed in a subglandular pocket by the same surgeon. MRI was carried out at least 12 months after surgery. None of the included women had any complaints about the implants and there were no clinical signs of capsular contracture. After the MIR examination of the implants in the supine position, the women were placed in the prone position with their breast hanging freely in a breast coil avoiding external compression to the breasts.

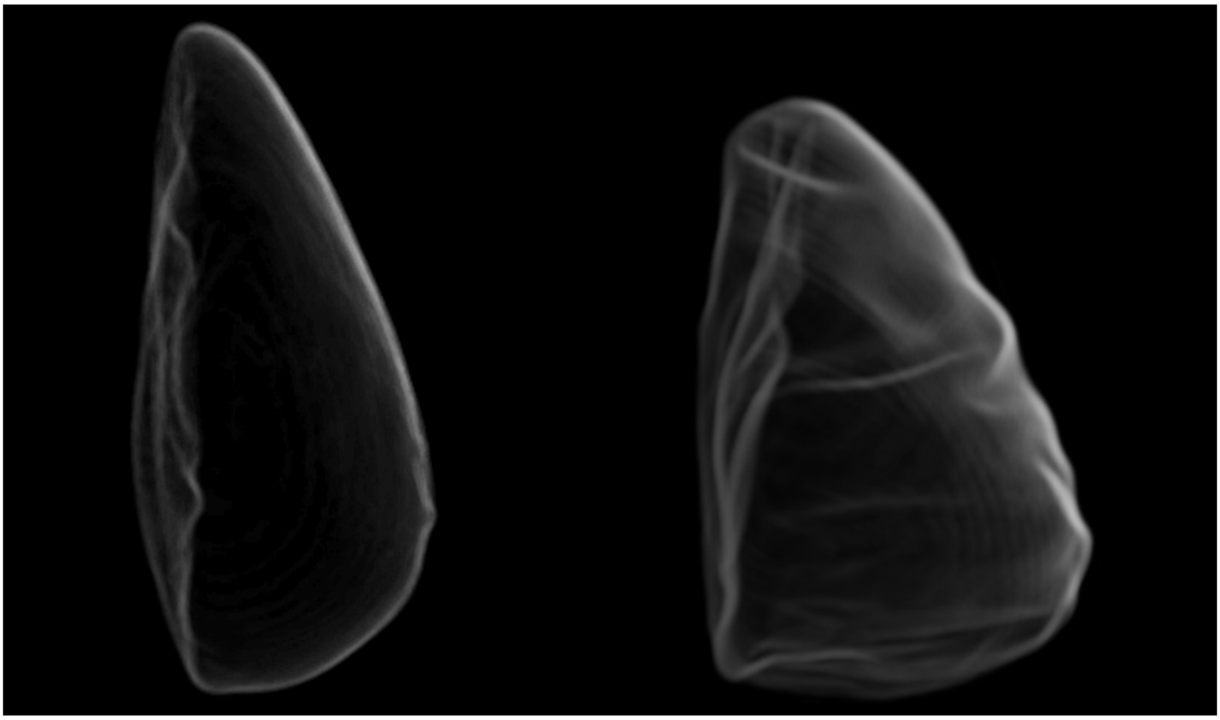

Figure 20 3D MRI reconstructions of the Style 410 breast implant in the supine (left) and prone (right) body position.

All implants had lower pole fullness in both the supine and prone position, confirming a typical characteristic of anatomical implant shape. However, for all implants the maximal anterior projection increased when the posture changed from supine to prone. This mean increase of almost 30 % was clearly visible on sagittal images and 3D reconstructions of the implants and breast surface renderings. In the supine position, the measured dimensions were almost similar to those specified by the manufacturer. In the prone position, the marked increase in projection came at the expense of height and width.

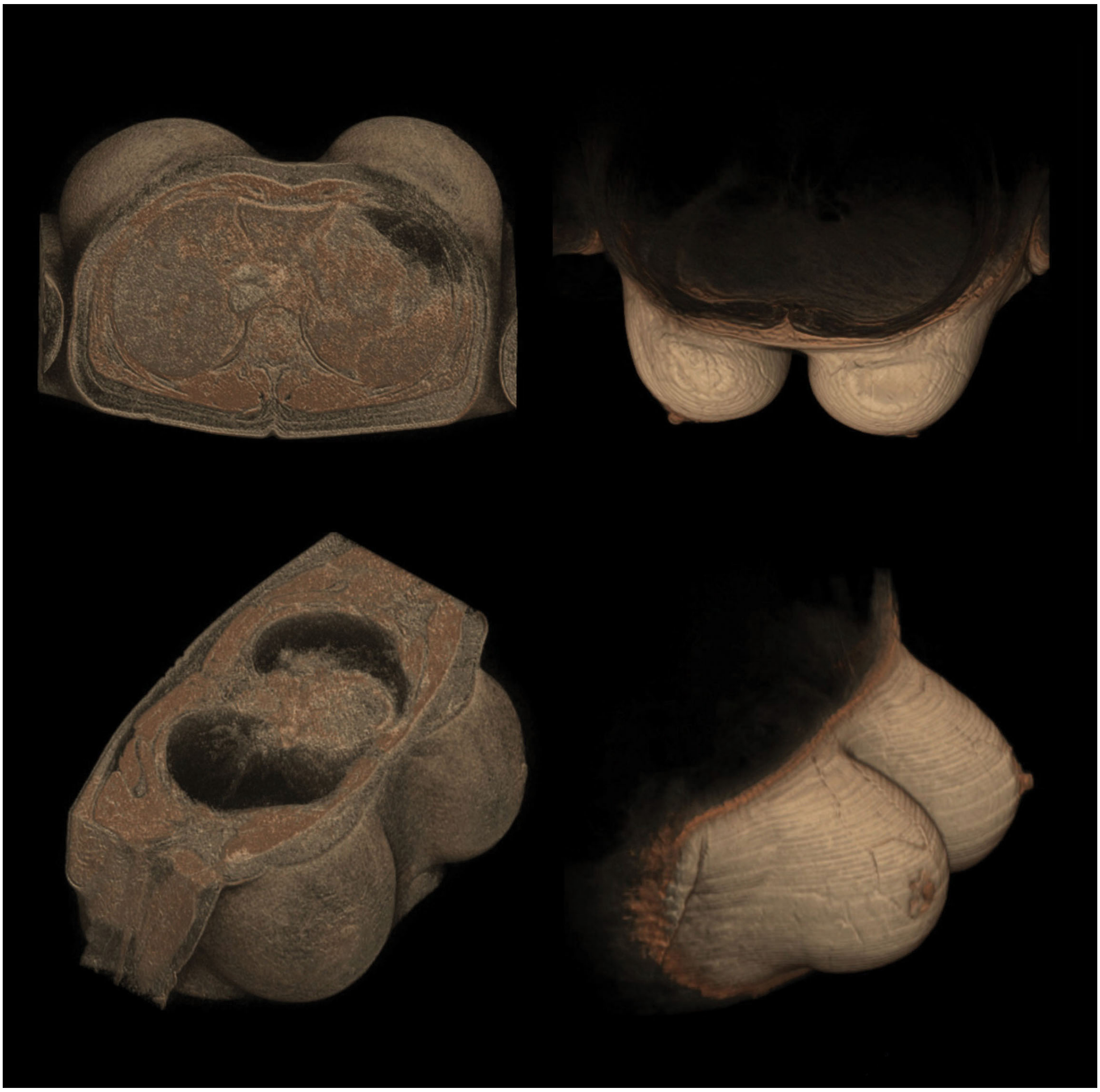

Figure 21 3D MRI surface rendering of the breasts in the supine (left) and prone (right) position visualizing that increased projection comes at the expense of height and width.

The Style 410 has been described as a form-stable implant. The results from our study show that in the supine position, the dimensions of the subglandularly positioned Style

410 implant were similar to the manufacturer's specifications. According to Bengtson's definition of a form-stable implant, one would expect the Style 410 to have the same dimensions in the prone position. However, the results from our study revealed that there was a marked increase in projection in the prone position. Therefore we cannot conclude that the Style 410 is form-stable if Bengtson's definition of a form-stable implant is used.

On the other hand, the results also show that this implant has its point of maximal projection in the lower pole in both body positions, which is a specific characteristic of anatomically shaped implants. So in a broader sense, one may say that the Style 410 is form-stable in the meaning that it keeps its anatomical shape in both body positions. This gives scientific support for the clinical observations made by several surgeons using this implant for breast augmentation and reconstruction. However, even though it may be correct to classify the implant as form-stable with respect to anatomical shape, it is not correct with respect to the dimensions.

From the surgeon's point of view, it is important to know that the Style 410 implant retains its anatomical shape after implantation and that it gives lower pole fullness to the breast. At the same time, the results from the study of paper IV show that the implant shell and the degree of silicone gel cohesivity allow the implant to adapt to body posture. Such plasticity of the so-called form-stable implant could be well appreciated by the patient as the implant in a natural way follows the form of the breast.

9. Discussion

The first three papers deal with breast reconstruction using autologous tissue, while the last paper focuses on the properties of a breast implant that is also widely used in breast reconstruction. All four papers illustrate the benefits of interdisciplinary collaboration between the plastic surgeon and radiologist. Breast reconstruction after treatment for mammary cancer is a demanding task that requires teamwork to achieve optimal results. Even though the plastic surgeon always will be the performing artist when it comes to the creation and shaping of the new breast, the radiologist may be an important fellow worker contributing in the development of new imaging methods that are valuable in the planning and implementation of reconstructive surgery. The radiologist may help to obtain increased knowledge on anatomy, physiology and the function of medical devices such as implants, and thereby providing a better basis for surgical decision-making.

9.1 Imaging in DIEP breast reconstruction

The use of CTA in DIEP breast reconstruction exemplifies the need for collaboration between plastic surgeons and radiologists. The surgeon's understanding of free flap surgery must be communicated to the radiologist, and the surgeon needs support from the radiologist's experience in the interpretation of cross-sectional images and 3D reconstructions. The implementation of new imaging protocols and reconstruction algorithms demands collaboration, not only between plastic surgeons and radiologists but also with radiographers.

Several authors have documented the benefits from implementing CTA in their preoperative planning of DIEP flap surgery, and this technique is now considered the gold standard by many authors. However, today's gold standard may not be the best possible solution tomorrow. CTA is inherently associated with ionizing radiation and the need for intravenous contrast injection, both significant risk factors that cannot be neglected. As several studies have documented the benefits of preoperative perforator imaging with CTA, these risks may be acceptable. Even though an alternative imaging technique such as color Doppler may provide much of the same information to the surgeon without these risk factors, many prefer not to use color Doppler because the examination is time consuming and highly operator dependent. The quest for a perforator imaging method with as little risk and few drawbacks as possible has been the motivational force behind the research in this thesis with respect to the use of DIRT in DIEP flap surgery.

Traditionally thermography is not considered a radiological modality, but medical thermography is certainly a medical imaging technique. In the Department of Radiology at the University Hospital North Norway, thermography has shown to fit well as an imaging modality. This has resulted in a dedicated thermography laboratory within the department. Much research may still be needed to establish medical thermography as a part of daily radiological practice. The experience and knowledge of radiologists may also be very helpful in research that may provide scientific documentation for the use of medical thermography and DIRT also in other areas than preoperative perforator mapping.

Often experimental research may be required to provide the necessary understanding of a new imaging technique. In an experimental setting many otherwise disturbing factors can be eliminated. By studying isolated abdominal flaps as described in paper I, the non-invasive and indirect DIRT technique for monitoring skin perfusion could be compared to the well-known invasive and direct technique ICG FA. However, by including traditional radiography after contrast injection in selected perforators the localization and branching pattern of the perforators were visualized as well. Although not described in the article, the use of CTA with 3D reconstructions provided even better visualization of the vascular anatomy in these isolated abdominal flaps. Comparing DIRT with CTA in this experimental setting showed for the first time that there was a clear relation between the distribution of hot spots on DIRT and the vascular anatomy visualized with CTA. This provided the inspiration to design studies to evaluate the usefulness of DIRT in a clinical setting.

The study in paper II reports on the clinical use of DIRT in preoperative mapping of perforators using intraoperative findings as the gold standard. All perforators chosen on the basis of DIRT turned out to be useful perforators confirmed by intraoperative findings and successful surgery. By adding preoperative CTA for 8 of the patients, it was possible to compare CTA with DIRT as well as with the intraoperative findings. In all these 8 patients the perforator selected on the basis of DIRT could be associated with a clearly visible perforator on CTA. The analysis of 8 patients with both CTA and DIRT functioned as a pilot study in preparation for the study reported in paper III.

The study in paper II gave a clear indication that DIRT may be a useful alternative to CTA in the preoperative planning of DIEP flaps, and the study reported in paper III gave additional support to choose DIRT as a reliable alternative to CTA. Even though DIRT does not visualize the location of all perforators visible on CTA, the results from the study show that DIRT is reliable in finding a suitable perforator for DIEP breast reconstruction. In addition to the static anatomical information provided by CTA, DIRT also provides valuable information on perforator hemodynamics. In summary the three first papers included in this thesis provide scientific support for using DIRT in the preoperative mapping of perforators. By choosing DIRT as an alternative to CTA one eliminates the main disadvantages of CTA, namely ionizing radiation and the use of intravenous contrast medium.

In the Department of Radiology at the University Hospital North Norway CTA has been used in the preoperative planning of perforator surgery for several years. CTA has been used as a gold standard in evaluating the usefulness of DIRT in the preoperative planning of perforator flaps. The results from the studies in paper II and III show that CTA provides detailed information on the branching pattern of the DIEA on both sides, the possible existence of an adequate SIEA as well as the localization and size of individual DIEA perforators. There is, however, concern about the radiation dose inherently correlated to CT examinations.

9.1.1 CTA and ionizing radiation

Rozen and Ashton write that the patient dose of a typical CTA perforator mapping is “less than 6 mSv, which is considerably less than a standard abdominal CT scan and is the dose associated with three abdominal plain films" [123]. In another publication Rozen stated that this dose is equivalent to only two plain abdominal radiographs [124]. It is correct that the dose may be larger than 6 mSv for many abdominal CT examinations. A regular CT of the upper abdomen may have a typical dose of 5-7 mSv while a complete abdominal and pelvic CT may have a dose of 8-14 mSv [125]. However, it is not correct that a dose of 6 mSv is only two or three times as high as the dose associated with an abdominal plain film.

According to Yu et al. the estimated ubiquitous background radiation per individual in the US population is 3.11 mSv per year [125], which means that the radiation dose associated with a preoperative CTA for perforator mapping as reported by Rozen equals approximately two years' background radiation. According to an article by Nguyen et al. the complete series of three abdominal plain films and one chest X-ray equals a total dose of 1.1 mSv [126]. Hart and Wall at the National Radiologial Protection Board in Britain write that an average abdominal X-ray is associated with a dose of 0.7 mSv, while a regular chest X-ray has a dose of 0.02 mSv [127]. This means that a CTA radiation dose of 6 mSv equals the dose of 8.5 abdominal, or 300 chest X-ray examinations.

One may ask if such a radiation dose is harmful to the patient. In addition we need to ask if the dose in real life may be higher than typically reported. Smith-Blindman et al. conducted a retrospective cross-sectional study describing the radiation dose associated with the 11 most common types of CT examinations performed on 1119 patients in the San Francisco Bay area [128]. They estimated the lifetime risks of cancer from the measured doses. They also documented higher and more variable doses than what is typically quoted from the most common types of CT studies used in clinical practice. Their results showed that a typical abdominal CT examination was associated with a 66 % higher dose than typically quoted and that the median dose of a multiphase abdomen and pelvic examination was almost 4 times higher. According to their estimates one out of 870 women at the age of 40 undergoing a typical CT examination of the abdomen and pelvis will develop a radiation-induced cancer. At the age of 20, the risk is almost doubled. If multiphase abdominal and pelvic CT is performed on 20 year-old women, one out of 250 will develop radiation-induced cancer.

9.1.2 CTA and the differentiation between arterial and venous perforators

Because CTA is performed in the arterial phase after intravenous contrast injection, many assume that the method is reliable in separating between arterial and venous perforators. Several authors claim that CTA can be used to measure the diameter of arterial perforators with high accuracy. It is common practice to evaluate the capacity of a perforator to supply the DIEP flap on the basis of its measured diameter on CTA. Different authors use varying minimum diameters between 0.5 and 1.5 mm for defining a “large” perforator [129]. Phillips et al. defined large-caliber subcutaneous perforators as perforators that have a diameter of 1 mm or more. Although Phillips used the word “perforators”, it is implied that they mean “perforator artery” as seen during the arterial phase of CTA. Such “large caliber arteries supply a greater volume of adipocutaneous tissue and represent better vascular pedicles” [3].

However, there are good reasons to ask if we really see what we think we see. A perforator consists of an artery and one or two comitant veins. Cina et al. reported a good agreement between the diameter measured as the sum of the perforating artery and vein with color Doppler and the presumed artery on CTA [45]. However, they found significant disagreement between the measured diameters of the arteries measured with color Doppler and CTA, as well as for CTA and intraoperative findings. Cina et al. postulated that the artery and vein run close together and, because of their small caliber and same opacity, these cannot be differentiated on CTA. Thus, measurement of the perforating artery on CTA may in fact constitute the sum of the diameters of the perforating artery and vein.

In an article published in 2006 Alonso-Burgos et al. showed examples of perforators presumably communicating with the superficial inferior epigastric artery [41]. When studying their figures we concluded that these periumbilical perforators most likely communicated with the superficial inferior epigastric vein, and not the artery. Our findings in paper III confirmed that this is often the case, as we observed several periumbilical perforators communicating with the superficial inferior epigastric vein. These perforators were large on CTA but did not produce hot spots on DIRT. We postulated that those perforators consisted of large veins and small arteries, which may illustrate the contribution of veins on CTA images, even though the CTA is acquired in the arterial phase.

Cina et al. gave a valuable contribution in their paper from 2010 on CTA versus color Doppler in the planning of DIEP breast reconstruction [45]. Their results showed that the sum of the diameter of the artery and vein with color Doppler was in agreement with the diameter of the presumed artery on CTA and significant disagreement between the diameters of arteries measured with color Doppler and CTA, as well as for CTA an intraoperative findings. Their findings indicate that the presumed artery on CTA may in fact constitute the sum of the perforator artery and vein. This may confirm that CTA actually visualizes a mixture of arterial and venous perforators, and that CTA as such may be misleading if we presume that we are studying arterial perforators only. Cina et al. recommended using color Doppler as the primary method for perforator mapping, and they recommended reserving CTA for selected cases only.

Recently we have added color Doppler to CTA and DIRT in the preoperative mapping of perforators, and we want to study the agreement between these three imaging methods. Our preliminary results are in agreement with the article by Cina et al., as we clearly see that CTA in many cases is unable to differentiate between arterial and venous perforators. Especially periumbilically we have seen large perforators with considerable venous flow communicating with the superficial inferior epigastric vein. These large veins seem to be associated with rather small arteries. The existence of such venous communications is also described by Carramenha e Costa et al. in an anatomic study [130] and nicely illustrated with the use of CTA by Rozen et al. in a study on the venous anatomy of the abdominal wall [131].

In our studies there were several cases with large periumbilical perforators on CTA that were not associated with bright hot spots on DIRT (paper III). Such indicates that these perforators do not transport much blood and therewith heat to the skin surface. We postulate that such a perforator consists of a large vein and a small artery. This postulation is supported by intraoperative findings and the fact that the 3D reconstructions in these cases show a connection between the perforator structure and the superficial inferior epigastric vein. In some cases it may therefore be inaccurate and even misleading to use perforator diameter on CTA as an absolute measure of the perforator's capacity to circulate a flap.

9.1.3 DIRT as an alternative to CTA in perforator mapping

The studies in this thesis show that DIRT is a useful method to localize reliable perforators for DIEP flap surgery. However, this does not imply that DIRT provides exactly the same information as CTA. The two methods are equally useful to localize an area of the abdomen where a useful perforator can be found during surgery. Other authors who have used DIRT in the preoperative mapping of perforators have confirmed the usefulness of this method [132, 133]. However, we do not fully agree with Chubb et al. writing about DIRT that "the technique matches the accuracy for perforator localization of CTA" [132]. According to our findings, hot spots on DIRT do not perfectly match the localizations where the perforators go through the anterior rectus abdominis fascia. Hot spots tend to be more laterally and in some cases more medially located due to the oblique course of perforators through the subcutaneous fat. Therefore we would rather say that DIRT is *accurate enough* to localize the area (or *quadrant* in paper III) in which a suitable perforator most likely can be found during dissection. The use of CTA may be more beneficial in cases where the surgeon wants more accurate information on the exact course of perforators though the rectus muscle. Such information may be especially helpful for inexperienced surgeons learning to do perforator flap surgery.

CTA is more accurate in relation to the exact localization of perforators, but DIRT provides useful additional information on the hemodynamics of each perforator. While CTA is a static imaging technique only visualizing anatomy, DIRT is a dynamic technique visualizing both the approximate localization as well as the function of individual perforators. A rapidly appearing hot spot with progressive rewarming indicates a well-developed vascular network around the hot spot. In this way DIRT may help to select a perforator that has a wide branching pattern, which is considered an important criterion when selecting a perforator for DIEP reconstruction [134].

Many papers report on the usefulness of CTA in mapping arterial perforators and most seem to take for granted that CTA acquisition in the arterial phase is a guarantee that only arteries are visualized. There is, however, a very short physical distance between arterial and venous perforators in the abdominal wall. Therefore this assumption may be erroneous. Probably most CTA examinations have significant venous overlap and many of the visualized vessels may in fact be contrast filled veins and not only arteries.

There is no doubt that CTA has become a valuable tool in the preoperative planning of perforator flap surgery. CTA provides information on DIEA branching pattern, the presence or absence of a usable SIEA as well as the distribution and diameter of different perforators. However, as Cina et al. have shown, we cannot always separate between arterial and venous perforators. Unless CTA is performed as a multiphasic examination, which would imply increased radiation dose, we get no dynamic information about flow in the perforators. What we get is a static picture of vessels with different diameters and degrees of attenuation reflecting the concentration of intravascular contrast medium.

Many consider CTA as the preferred modality for all patients undergoing perforator flap surgery, but there are several alternatives that may complement or even substitute CTA in this area. Color Doppler is an operator dependent and quite time-consuming examination, but the technique provides accurate information on the diameter and flow of individual perforators. DIRT does not provide detailed anatomic information, but allows for a dynamic evaluation of perforator function by observing the characteristics of individual hot spots. Dynamic MRI may also become an important alternative to CTA in the preoperative planning of perforator flaps. Even though MRI may not have the same spatial resolution in the evaluation of mall perforators, multiple acquisitions may be performed to obtain dynamic information on flow without the use of ionizing radiation.

Even though CTA has been proven to be a valuable tool in the preoperative mapping of perforators, the method is not flawless and may actually give a false impression of large arterial perforators in cases with a large vein and small artery. On the other hand, DIRT does not visualize the perforators directly, but rather visualize the effect of each individual perforator. Each hot spot is the result of a perforator’s artery and vein, as both are needed to produce a rapidly appearing hot spot. We believe that paper I, II and

III provide important contributions to the scientific documentation needed to replace CTA with DIRT in the preoperative mapping of perforators. Today's gold standard may not be the gold standard of tomorrow, and DIRT can certainly become the successor of CTA even though CTA still may be preferred in cases with altered anatomy after trauma or abdominal surgery.

A vast number of papers have been published on medical thermography, but more scientific documentation is needed to support the use of this technique in daily clinical practice. Through our own research, such documentation has now been provided for routine clinical use of thermography in breast reconstruction with a DIEP flap. Paper I in this thesis reports an experimental study comparing DIRT with ICG FA, while paper II and III both address clinical use of DIRT in the preoperative planning of DIEP flap surgery. Other research papers published by our group conclude that DIRT is a useful method for intraoperative anastomosis control as well as postoperative monitoring of flap perfusion [107, 135, 136]. The use of DIRT has also provided new and interesting insights on perfusion dynamics of free flaps in the postoperative phase [137].

9.2 Form stability of the Style 410 implant

Paper IV deals with a quite different problem than the previous papers. However, this paper also illustrates the need for interdisciplinary collaboration in plastic surgery. Several other articles have addressed the postoperative results obtained with the Style 410 anatomically shaped implant, but none of these use objective data as those obtained with MRI acquired in two different body positions. Nipshagen et al. used MRI and described the static properties of the implant in the supine position, but they did not address the issue of form stability [85].

The Style 410 implant has been described as *form-stable*, a term without any widely accepted definition. In their core study, Bengtson et al. defined a form-stable implant as "an implant that will maintain its dimensions and form in any position" [11]. In our study 9 women with Style 410 silicone implants were examined with MRI in both the supine and prone position. The results showed that the implants *do not* keep their dimensions when the MRI is performed with the patient in the prone position. The implants' projection increased with an average of almost 30 % at the cost of height and width. However, the implants still had their maximum projection in the lower pole in both positions, which means that they still had lower pole fullness, which may be a desirable characteristic in resemblance of a natural breast. With a regular closed MRI scanner the women could not be examined in the upright position. We assumed that the implants in an upright position would show a projection in the lower pole between that of the supine and prone position.

In a pilot study included in the discussion article following the publication of paper IV in *Plastic and Reconstructive Surgery*, Dennis Hammond actually performed MRI in the upright position in an open MRI scanner. He confirmed our assumption and commented that "similar cohesive silicone gel implants (Style 410) have been imaged, and the findings of this preliminary study support completely the observations made by Weum et al." [138]. Hammond concluded his discussion article by stating, "In summary, this article is a welcome addition to the implant literature. The findings related to maintenance of anatomical implant shape in situ lend convincing and much needed credible scientific support to the anatomical concept as it applies to aesthetic and reconstructive breast surgery."

In a later issue of *Plastic and Reconstructive Surgery*, the inventor of the Style 410 implant, John B. Tebbetts commented on our article. He addressed our evaluation of form stability with MRI and wrote: "This article subjects patients to magnetic resonance imaging to show what any surgeon who has ever held a 410 in hand should be able to see with the naked eye - no version of the device is completely form-stable or ever has been" [139]. In our reply to his letter to the Editor we agree that any surgeon may evaluate with "the naked eye" the degree of stiffness or form stability the silicone gel of the Style 410. This would, however, be a purely subjective evaluation without the objective qualities of a scientific study. Tebbetts also wrote: "Magnetic resonance imaging reconstructions have never been proved to accurately represent postoperative results." However, MRI is an excellent method to visualize breast implants and provides detailed information on their three-dimensional form and dimensions. In paper IV MRI provided objective reproducible data on the form and dimensions of implants which makes scientific evaluation possible.

In our reply to Dr. Tebbetts we addressed the lack of a proper definition of “form-stable” even though this term has been circulating in plastic surgery articles for almost a decade, including several articles written by himself [140]. Until Bengtson et al. published their core study on the Style 410 breast implant in 2007 there were to our knowledge no scientific articles that provided a definition of the term “form-stable”. As Bengtson et al. defined form stability as maintenance of implant form and dimensions in any position, our study revealed that Style 410 does not fulfill these criteria. This may also be important as the core study is used as documentation for a possible FDA approval of Style 410 for general use in the United States. In our answer we wrote: “Given the results from our study, we do not feel that there is a need to come up with a more accurate definition. We feel that the use of the term form-stable as related to the Style 410 should be avoided, as it may cause confusion.” However, Style 410 is still anatomically shaped in at least the supine, prone and upright positions. And the degree of cohesivity may be an advantage as the implant is able to adapt to body posture in much the same way as a natural breast.

10. Clinical implications and future considerations

The studies reported in paper I, II and III were designed to evaluate DIRT as a method for preoperative planning of DIEP flap surgery. Even though CTA is now considered the gold standard for perforator mapping, the results from our studies support the use of DIRT as an alternative to CTA. DIRT provides all the necessary information about the localization of useful perforators for DIEP flap surgery. In addition, we get useful information on the hemodynamics of individual perforators. Probably the sum of this information is more valuable than the exact localization of perforators achievable with CTA. DIRT gives no ionizing radiation and does not include the use of contrast media. In our experience the results from DIRT are easier to interpret than the results of CTA and color Doppler. The method is easy to perform with equipment that has reasonable price when compared to CT and ultrasound equipment. The examination may be repeated with consistent results. A natural consequence will be to replace CTA with DIRT on a greater scale also in other hospitals around the world. To the degree that plastic surgeons and radiologists become convinced that DIRT is a useful alternative to CTA, more research can be performed to explore the possibilities and limitations of DIRT in preoperative perforator mapping.

Other plastic surgeons and researchers have also shown interest in using DIRT for perforator mapping. Recently a group at Royal Melbourne Hospital & Taylor Laboratories published a correspondence and communication article in *the Journal of Plastic, Reconstructive and Aesthetic Surgery* on the use of DIRT in the preoperative planning of microsurgical breast reconstruction [133]. They rightly claim that their group has been highly influential in the elucidation of CTA in perforator mapping. However, they also claim to describe the first case (at least to their knowledge) of DIRT in comparison to CTA in DIEP flap surgery. We felt obligated to answer their communication with a letter to the Editor explaining that we were astonished as we in 2009 published an article where DIRT was compared with CTA [141]. In the *Toolbox for Autologous Breast Reconstruction* issue of Clinics in Plastic Surgery, guest Editor Maurice Y. Nahabedian refers to our study as the first clinical study on DIRT in perforator flap surgery [142]. The group from Melbourne also published another manuscript in Annals of Plastic Surgery 2011 recommending DIRT as an alternative to CTA without any references to formerly published articles [132]. The authors wrote that they recently had introduced digital thermography as technique to highlight the location of perforators. We responded to their paper reminding that this technique has been known since 1986 when Theuvnet et al. used thermography to localize perforators [135].

We were surprised that this group published two papers almost simultaneously without referring to the work already done on DIRT and perforator flap surgery. We are, however, happy that more researchers are discovering the benefits of DIRT in preoperative perforator mapping. Dr. Rozen and the Melbourne group have been pioneers in the development of CTA in this area, and we welcome their future contributions to the research on DIRT. In the same article, this group concluded that in their experience thus far, the technique matches the accuracy for perforator localization of CTA, and a larger clinical trial of the technique is currently underway.

There is certainly a need for reliable methods without ionizing radiation and contrast injection. MRI angiography may as such be a good alternative to DIRT in the future. Until now the results of MRI have been promising but still less reliable than CTA.
With the documentation now provided, DIRT is a good alternative to CTA in the preoperative mapping of perforators. DIRT is also a useful method for intra- and postoperative monitoring of flap perfusion [107, 136, 143]. As such DIRT is a promising method for many situations were monitoring of temperature changes can provide useful information on tissue perfusion.

The study on the Style 410 implant was motivated by a desire to obtain objective information about the postoperative behavior of the implant. Such information is valuable in the preoperative planning of breast augmentation and reconstructive surgery with breast implants. Such knowledge may help to inform the patient on the possible postoperative outcome and aesthetic result. Knowledge about the shape and dimensions of normal implants may also be useful when evaluating MRI of patients with possible capsular contracture. Probably an MRI study on Style 410 with capsular contracture in different body positions would reveal another form and other dimensions than the results reported in this study, as capsular contracture tend to make implants more round and less able to adapt to external pressure and gravitation.

All such research is a product of interdisciplinary collaboration. I expect much exciting research to emerge in the borderland between plastic surgery and radiology in the days to come.

11. Conclusions

Paper I

The extent of the perfused skin area indicated by the indirect DIRT technique corresponds well with the perfused skin area indicated by the direct ICG FA technique. In experimental situations DIRT is a good alternative to ICG FA for visualization of skin perfusion.

Paper II

Preoperative perforator selection and planning of DIEP flaps is facilitated with the use of DIRT. The technique is noninvasive and easy to use. DIRT allows for qualitative assessment of perforators to the DIEP flap and therewith providing valuable information that helps in planning and designing this flap.

Paper II

The close association between the location of first appearing hot spots with DIRT and perforators with CTA combined with information on perforator hemodynamics obtained with DIRT makes DIRT a good alternative to CTA in perforator selection in DIEP breast reconstruction. DIRT does not require the use of ionizing radiation or contrast medium.

Paper IV

The Style 410 implant is described as a form-stable, anatomically shaped, cohesive, silicone gel–filled implant. However, its shell and the degree of silicone gel cohesivity allow for a change in form depending on body posture. Compared with the supine position, there was a marked increase in implant projection in the prone position. The Style 410 implant keeps its lower pole fullness after subglandular implantation in both the supine and prone positions. This lower pole fullness is described as a characteristic for anatomically shaped breast implants.

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