Simulation Study for Mammography Using Photon Counting Detectors in High Resolution Whole-Body Computed Tomography

Master’s Thesis of

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Karlsruhe, 02.11.2017

(Madeleine Hertel)
Abstract

High-resolution detectors have already been investigated in the context of dedicated breast computed tomography (CT) scanners. These systems turned out to be capable of reliably detecting microcalcifications and tissue malignancies at the required spatial resolution and acceptable patient dose levels. The arrival of photon-counting detectors (PCD) in whole-body clinical CT scanners shifts the spatial resolution capabilities of these systems towards the range required for 3D breast imaging.

This thesis provides a CT image simulation study in order to assess the resolution capability of typical whole-body CT scanners equipped with PCDs, and to investigate whether microcalcifications and tissue malignancies could be detected at dose levels typically applied in thorax CT scans.

The simulation used a recently developed analytical detector model for PCDs, providing a realistic detector response function and accounting for effects such as spatio-energetic cross talk between pixels. Experimental calibration and validation of this model with measurements from a real whole-body prototype CT scanner with PCD was the first part of this work. Comparison of image properties such as image noise and contrast reproduction of material probes showed reasonable agreement and justified the use of this model to investigate the detectability of breast cancer in whole-body PCD CT. Under variation of detector pixel size and focal spot profile of the x-ray tube a synthetic thorax phantom with realistic contrast values of the calcifications was investigated.

In this work, the distinct improvement of achievable spatial resolution using PCDs compared to conventional CT systems could be demonstrated. The required spatial resolution of around hundred micrometer can be reached with realistic system designs. However, the resulting image noise at dose levels regularly used in CT examinations of the thorax is too high to allow reliable detectability of small microcalcifications. In conclusion, dedicated breast imaging systems remain modality of choice for the task of reliable breast cancer screening.
Zusammenfassung

Bereits in früheren Studien wurde die Verwendung hochauflösender Detektoren in speziellen Computertomographen (CT) erforscht, deren Geometrie explizit für die Bildgebung der weiblichen Brust ausgelegt ist. Solche Systeme erlauben einen zuverlässigen Nachweis von Mikroverkalkungen und bösartigen Gewebeveränderungen bei Erreichen der notwendigen Ortsauflösung und bei akzeptabler Patientendosis. Mit der Einführung photonenzählender Detektoren in die Ganzkörper-CT wird das Auflösungsvermögen dieser Systeme nun erheblich erhöht, so dass diese für die 3D Bildgebung der weiblichen Brust in Frage kommen könnten.

Gegenstand dieser Arbeit ist eine Bildsimulationsstudie für Ganzkörper-CT Systeme, die mit photonenzählenden Detektoren ausgestattet sind. Dabei wird nicht nur das resultierende Auflösungsvermögen dieser Systeme untersucht, sondern auch evaluiert, inwieweit Mikroverkalkungen und bösartige Gewebeveränderungen detektiert werden können, wenn eine ähnliche Patientendosis wie in üblichen Thorax-Untersuchungen verwendet wird.


In dieser Arbeit konnte eine deutliche Verbesserung der maximal erreichbaren Auflösung durch Verwendung photonenzählender Detektoren im Vergleich zu konventionellen CT-Detektoren gezeigt werden. Die benötigte Auflösung von circa hundert Mikrometern kann mit realistischen Systemauslegungen durchaus erreicht werden. Dennoch war unter Verwendung von für Thorax-Untersuchungen üblichen Patientendosiswerten das resultierende Bildrauschen wesentlich zu hoch, um die Detektion kleiner Mikroverkalkungen noch zu gewährleisten. Lediglich Mikroverkalkungen mit einem Durchmesser von 250 µm oder mehr können zuverlässig erkannt werden. Somit lässt sich zusammen-
fassend sagen, dass die speziell für die Brust-Bildgebung entwickelten Verfahren nach wie vor Mittel der Wahl bei der Brustkrebsvorsorge sind.
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Acronyms

ASIC Application-Specific Integrated Circuits.

CT Computed Tomography.

DCIS Ductal Carcinoma in Situ.

ER Estrogen Receptor.

FBP Filtered Backprojection.

FoV Field of View.

HER2 Human Epidermal Growth Factor Receptor 2.

HU Hounsfield unit.

IDC Invasive Ductal Carcinoma.

ILC Invasive Lobular Carcinoma.

LCIS Lobular Carcinoma in Situ.

MRI Magnetic Resonance Imaging.

MTF Modulation Transfer Function.

NOS not other specified.

PCD Photon-Counting Detector.

PDF Probability Density Function.

PR Progesterone Receptor.

PSF Point Spread Function.

ROI Region of Interest.

SRF Spectral Response Function.
Acronyms

TNM  Tumor-Node-Metastasis.

WFBP  Weighted Filtered Backprojection.
1. Introduction

Breast cancer is one of the most common diagnosed cancers worldwide, accounting for approximately 25% of all cancer cases in women [30, p. 362]. Highest incidence rates are found in countries with advanced human development and are therefore associated with the Western lifestyle; further risk factors include early menarche and late or no childbirth [35, p. 9].

Pathology of Breast Cancer

Breast cancer is not a single disease, it is a heterogeneous set of diseases which differs morphologically and clinically in response to treatment [30, p. 362].

Generally, tumors arise mostly in epithelial cells in glandular tissue which includes milk ducts (ductal carcinoma) or lobules (lobular carcinoma). The tumors can be distinguished into groups of in situ and invasive lesions. Precursor (in situ) lesions are malignant epithelial proliferations which are still confined to the tissue of origin. They have an inherent tendency for progression to invasive breast cancer. Invasive lesions are malignant epithelial cells which have already invaded the surrounding tissue and have the inherent ability to metastasize. [30, 363 ff.].

Precursor Lesions

In general, noninvasive lesions can be subdivided into two broad categories: Ductal Carcinoma in Situ (DCIS) and Lobular Carcinoma in Situ (LCIS) (see Figure 1.1). The goal of the therapy of such lesions is preventing the development of invasive cancer while minimizing the the side effects of the treatment.

DCIS is not necessarily a precursor lesion for invasive breast cancer but it is associated with histological findings which show an increased risk for subsequent development of invasive carcinoma. Therefore, no specific treatment is indicated similar to the approach of patients with other high-risk characteristics. In most cases the detection is based on the presence of microcalcifications associated with these lesions. Up to 30% of all detected malignancies can be allocated to DCIS. [35, p. 68]

LCIS is an epithelial proliferation with cellular aberration and an inherent tendency for progressing to invasive cancer. Despite the fact that the lesion is lobular, a possible subsequent cancer is more likely to be ductal. Depending on the size of the lesion, a partial to total mastectomy is usually required and mostly curative [35, p. 67]. Chances of
1. Introduction

recurrence can be significantly reduced by subsequent radiation therapy with or without addition of hormonal therapy (e.g. tamoxifen). [14, 9 f.]

![Precursor lesions. (a) LCIS with characteristic confined cell proliferation (b) DCIS with confined atypical cell proliferation and microcalcifications [35]](image)

Invasive Breast Cancer

An Invasive Ductal Carcinoma (IDC), not other specified (NOS) is a heterogeneous group of tumors which can not easily be classified due to a lack of precise criteria. Ductal NOS form the largest group of invasive breast cancers comprising approximately 70% of all diagnosed carcinomas [35, p. 20].

An Invasive Lobular Carcinoma (ILC) characterizes a proliferation of non-cohesive individual cells dispersed in a fibrous tissue or in single-file linear pattern in the stroma (Figure 1.2 B). Due to their diffuse growth pattern ILC is a poorly delimited carcinoma and represents about 10% of invasive breast cancers.

![Invasive breast cancers. (a) IDC invaded surrounding tissue. (b) ILC with characteristic single-file linear pattern [35]](image)
Classification of Tumors

For patient prognosis and discussing treatment, tumors are divided into histological grades as well as assigned to a specific stage [14, p. 5]. The grading system of tumors is based on the assessment of tubule formation, nuclear pleomorphism and mitotic counts (proliferation). As shown in Table 1.1, each parameter is given a score (1-3) and the scores are added to classify the tumors into grades, from low grade (grade 1): well differentiated to high grade (grade 3): poorly differentiated. This categorization is recognized as a powerful prognostic factor and indicator for further treatment [30, p. 365].

Table 1.1.: Grading system of tumors [35]

<table>
<thead>
<tr>
<th>Feature</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tubule and gland formation</td>
<td></td>
</tr>
<tr>
<td>majority of tumor (&gt; 75%)</td>
<td>1</td>
</tr>
<tr>
<td>moderate degree (10 - 75%)</td>
<td>2</td>
</tr>
<tr>
<td>little or none (&lt; 10%)</td>
<td>3</td>
</tr>
<tr>
<td>Nuclear pleomorphism</td>
<td></td>
</tr>
<tr>
<td>small, regular uniform cells</td>
<td>1</td>
</tr>
<tr>
<td>moderate increase in size and variability</td>
<td>2</td>
</tr>
<tr>
<td>marked variations</td>
<td>3</td>
</tr>
<tr>
<td>Mitotic counts</td>
<td></td>
</tr>
<tr>
<td>≤ 7 mitoses per 10 high power fields</td>
<td>1</td>
</tr>
<tr>
<td>8-14 mitoses per 10 high power fields</td>
<td>2</td>
</tr>
<tr>
<td>≥ 15 mitoses per 10 high power fields</td>
<td>3</td>
</tr>
<tr>
<td>overall grade</td>
<td></td>
</tr>
<tr>
<td>Grade 1: 3-5</td>
<td></td>
</tr>
<tr>
<td>Grade 2: 6-7</td>
<td></td>
</tr>
<tr>
<td>Grade 3: 8-9</td>
<td></td>
</tr>
</tbody>
</table>

The histopathological analysis also provides the stage of disease using the Tumor-Node-Metastasis (TNM) classification system for breast cancer. In Table 1.2 an excerpt of the basic system is listed, the complete classification table is attached in Section A.1. T(0-4) describes the size of the tumor, N(0-3) whether or which lymph nodes are involved and M(0-1) if metastasis have spread to the surrounding tissue [14, 6 ff.]. The TNM classification then helps determining the stage of the tumor (see Table 1.3). In addition, hormonal response to Estrogen Receptor (ER), Progesterone Receptor (PR) and Human Epidermal Growth Factor Receptor 2 (HER2) are assessed using immunohistochemistry [30, p. 366].
1. Introduction

Table 1.2.: Extract of the TNM classification system [35]

<table>
<thead>
<tr>
<th>Primary Tumor (T)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>TX: primary tumor cannot be assessed</td>
<td></td>
</tr>
<tr>
<td>T0:</td>
<td>no evidence of primary tumor</td>
</tr>
<tr>
<td>T1:</td>
<td>tumor 2 cm or less in greatest dimension</td>
</tr>
<tr>
<td>T2:</td>
<td>tumor more than 2 cm but not more than 5 cm in greatest dimension</td>
</tr>
<tr>
<td>T3:</td>
<td>tumor more than 5 cm in greatest dimension</td>
</tr>
<tr>
<td>T4:</td>
<td>tumor any size with direct extension to chest or skin</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Regional Lymph Node (N)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>NX:</td>
<td>regional lymph nodes cannot be assessed</td>
</tr>
<tr>
<td>N0:</td>
<td>no regional lymph node metastasis</td>
</tr>
<tr>
<td>N1:</td>
<td>metastasis to movable ipsilateral axillary lymph node(s)</td>
</tr>
<tr>
<td>N2:</td>
<td>metastases in ipsilateral axillary lymph nodes fixed or matted, or in clinically apparent ipsilateral internal mammary nodes in the absence of clinically evident axillary lymph node metastasis</td>
</tr>
<tr>
<td>N3:</td>
<td>metastases in ipsilateral infraclavicular lymph node(s) with or without axillary lymph node involvement, or in clinically apparent ipsilateral internal mammary node metastasis; or metastasis in ipsilateral supraclavicular lymph node(s) with or without axillary or internal mammary lymph node involvement</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Distant Metastasis (M)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>MX:</td>
<td>distant metastasis cannot be assessed</td>
</tr>
<tr>
<td>M0:</td>
<td>no distant metastasis</td>
</tr>
<tr>
<td>M1:</td>
<td>distant metastasis</td>
</tr>
</tbody>
</table>

Table 1.3.: Extract of the TNM staging system [35]

<table>
<thead>
<tr>
<th>Stage Grouping</th>
<th>Tis (in situ)</th>
<th>N0</th>
<th>M0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 0</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage I</td>
<td>T0</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIA</td>
<td>T2</td>
<td>N1</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIB</td>
<td>T0</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N1, N2</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIA</td>
<td>T4</td>
<td>N0, N1, N2</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>any T</td>
<td>any N</td>
<td>M1</td>
</tr>
</tbody>
</table>
**Treatment of Breast Cancer**

Primary goal treating breast cancer is controlling the disease to achieve cure. In addition, it should improve the patient’s survival, minimize the risk of metastasizing and recurrence as well as reducing side effects [24]. Therapy modalities comprise surgery and radiation therapy as well as systemic therapy like cytotoxic (chemo)therapy, hormonal therapy and targeted therapy at HER2. Depending on the stage of the tumor, different therapies are combined. [35, 11 ff.]

Early stage breast cancer (T1) with tumors smaller than 1 cm is usually treated with mastectomy or breast conservation therapy (e.g. lumpectomy - excision of tumor conserving the breast) with subsequent irradiation. Systemic therapy is mostly not required, whereas cytotoxic adjuvant chemotherapy is appropriate for tumors larger than 1 cm. Hormonal therapy is also recommended if the tumor is hormonal-receptor-positive. Follow-up is usually performed annually including screening and physical examination.

Intermediate to advanced stage cancers are initially treated with preoperative, also called neoadjuvant, chemotherapy. Tumors of stages T2 larger than 4 cm and T3 without fixed axillary node involvement are operable. Total mastectomy with axillary lymph node dissection is performed. Afterwards it is treated like early stage cancer, hormonal therapy, if receptive, is used for at least five years. Tumors stages of T3 and higher are inoperable. If the patient responds well to chemotherapy, the tumor can become operable. Advanced breast cancers are additionally irradiated. [14, p. 15]

**Breast Imaging Modalities**

Breast imaging modalities are important for breast cancer screening, the classification and sampling of non-palpable breast abnormalities as well as for defining the extent of the breast tumor [14, p. 84]. In the following the most important breast imaging techniques are introduced.

**Mammography**

Mammography is a projection based x-ray imaging method creating two-dimensional images of the breast with a resolution up to 80 µm [35, p. 69]. It is the most common screening modality [30] with the goal of early detection of breast cancer through characteristic masses and microcalcifications. To acquire a mammogram, the breast is compressed in a dedicated mammography unit to achieve an uniform as well as a smaller object thickness. This causes less scattered radiation and motion blurring by penetration resulting into better image quality. The introduction of digital mammography further improved the image quality allowing image manipulation for better detection and therefore possible dose reduction. In screening mammography, usually two images from different angles are taken: top-to-bottom view (craniocaudal) and an angled side view of 45° (mediolateral oblique). In the case of abnormal findings, further diagnostic mammograms are taken as well as additional images from other modalities like sonography or...
1. Introduction

Magnetic Resonance Imaging (MRI). Although screening mammography in women between the age 45 and 69 is recommended annually to every two years, e.g. by the German [21] or American Cancer Society [28], its efficacy stays controversial. Mammography is also limited in imaging dense breasts because overlapping tissue can hide lesions. [14, 83ff.]

Mammography is also the most important method for the detection of DCIS, which comprises up to 30% of all detected malignancies [35, p. 68]. The detection is based on the presence of significant microcalcifications associated with these precursor lesions. Calcifications also provide information on the extent of the lesion, which is important for further treatment. In well differentiated DCIS the calcifications are of the crystalline type and show a multifocal distribution. In contrast, the calcifications in poorly differentiated DCIS appear in linear or branch-like clusters, following the arrangement of the ducts (see Figure 1.3).

![Figure 1.3.: Mammograms of microcalcifications indicating DCIS. (a) Highly suspicious course of granular and microcalcifications, which follow the ductal course. (b) High grade DCIS with characteristic fragmented, branching calcifications. [35, p. 68]](image)

Tomosynthesis

Tomosynthesis is an advanced form of mammography imaging providing pseudo-three-dimensional images of the breast. It is a limited-angle x-ray tomography modality at dose levels comparable with projection based imaging. Thereby the x-ray tube moves in an arc over the compressed breast, capturing multiple images of different angles. The detector is moved simultaneously in opposite direction, as illustrated in Figure 1.4. The images are synthesized in a set of slices (cross section images) resulting in a pseudo-three-dimensional image. In comparison to mammography, tomosynthesis provides a higher diagnostic accuracy especially in dense breasts. The pseudo-three-dimensional images can minimize the tissue overlap which can hide lesions or help distinguish overlapping tissue from tumors. [8, 179ff.]
Sonography and MRI

Sonography (medical ultrasound) and Magnetic Resonance Imaging (MRI) are both complementary imaging techniques to support the diagnosis of breast cancer. Sonography is based on the different propagation velocities of ultrasound waves in different materials. Ultrasonic images, so called sonograms, are created by sending pulses of ultrasound into tissue by using a probe and recording the echoes of the signal. In the most used B-mode (brightness mode), the amplitude of the sound wave echoes are converted to gray values and displayed as images. Sonography is routinely used in examinations due to its harmless, non-ionized radiation. It can provide additional information of breast lesions which cannot be visible or revealed on mammography and distinguish benign from malignant lesions. Due to its real-time imaging capability it is also the best imaging modality to guide interventional procedures like needle biopsy on breast masses. Hence, ultrasound cannot detect microcalcifications and its efficiency is operator dependent. Although it provides advantages like detecting non-palpable breast masses, its efficacy is controversial. [14, 121ff.]

Since its introduction in the 1980s, MRI developed to an important medical imaging technique. Compared to x-ray projection imaging or Computed Tomography (CT) high quality cross section images of the body can be obtained without using ionized radiation. MRI images feature a high soft tissue contrast as well as the ability to choose an arbitrary image plane. By applying a strong magnetic field, some atoms with a dipole moment alter their magnetization alignment relative to the field. Turning off the field, the protons align again with the static magnetic field and thereby emit a radio frequency signal. The relaxation time is characteristic for each material and therefore determines the contrast between different tissues. For breast imaging purposes, MRI plays an important role in screening women at high risk of developing breast cancer and defining the extent of a malignant breast tumor. In addition, MRI can reveal multicentric and multifocal carcinoma which cannot be seen on mammography or sonography, especially
1. Introduction

in dense breasts. The potential disadvantages of MRI are its limited utility in detecting microcalcifications and taking more time than mammography or sonography. Also it is involved with increased costs. [14, 110ff.]

Breast CT Using Photon Counting Detectors

Digital mammography is a widespread method for breast cancer screening but is not considered a perfect solution, especially for dense breasts. Also tomosynthesis is limited in its three-dimensional resolution. CT would provide a high three-dimensional resolution but is limited in spatial resolution. To overcome these limitations, a concept for dedicated breast CT was introduced. Thereby, a PCD is implemented in x-ray CT which allows high spatial resolution of 100 µm and better. The breast CT showed sufficient 3D resolution to have reliable detectability at average glandular dose levels, so the technology is considered a potential alternative solution for breast imaging. [17]

Figure 1.5.: Breast CT imaging geometry using PCD so that one breast at a time can be scanned. Thereby only the breast is in the scan range. Image from [17]

Mammography in Whole-Body CT

In comparison to conventional CT systems, PCDs provide a distinct higher resolution. As already introduced above, PCD in dedicated CT breast imaging enables resolutions up to 100 µm. The question to be investigated in this work is if, with the advent of PCDs, a similar resolution can be achieved in whole body CT. This could be realized for instance with dedicated scan modes for breast imaging. Also, breasts are frequently inside the scanned range for routine examinations of the lung or heart. These routine scans could provide clinically useful information about potential pathologies in the breast. Additionally, in contrast to common screening methods, a CT scan has the possibility to include the region between the breast towards the shoulders, where most cancers arise (see Figure 1.6) [35, p. 17]. Whole body CTs also offer a more comfortable imaging position while both breasts can be scanned at the same time, see Figure 1.7. The high resolution capability of PCD in could provide the necessary performance of around 100 µm for breast examination [35, p. 69] and therefore additional diagnostic value.
First, a new detector model for PCD simulations is validated with prototype measurements. This model is later used to investigate the resolution capability of a whole body CT scan at dose levels comparable to regular thorax scans.

Figure 1.6.: Probability of occurrence of tumors in the breast. Most tumors arise in the upper outer quadrant towards the shoulders. Numbers from [35, p. 17]

Figure 1.7.: Patient scanned in a whole-body CT where the complete thorax is in the scan range and both breasts can be scanned at the same time [11]
2. Computed Tomography

Computed Tomography (CT) has evolved into one of the most important imaging methods in medical diagnostics. It was the first method to acquire cross-section images of the human body without superposition of anatomical structures. CT is based on the rectilinear propagation of x-rays and their attenuation passing an object. With these projections a reconstruction of the original object is possible. The word tomography derives from the Greek τομή (tomé) 'section' and γράφω (grápho) 'to write'.

The fundamental mathematics underlying CT image reconstruction were described by Johann Radon in 1917 [23]. He solved the inverse problem of reconstruction by showing that the spatial structure of an object can be derived from its projection data. Allan McLeod Cormack eventually contributed 1963 the first mathematical implementation for tomographic reconstruction [7]. Nearly ten years later, 1972, the first CT scanner was introduced by Sir Godfrey Newbold Hounsfield [13]. For their achievements Cormack and Hounsfield received a Nobel Prize in Physiology or Medicine in 1979 [4].

The CT systems of the first generation were so called translation-rotation scanners [10]. A pencil beam allowed only single detector elements to be irradiated, so a translation of the tube was needed to record a complete projection set (see Figure 2.1). The acquisition of the data took several minutes which could lead to severe deterioration of the image quality in the form of motion artifacts due to the movement of the patient[16]. The second generation already used a narrow fan beam to illuminate a small group of detector elements. The translation of the tube was still required but the acquisition time was reduced. The third generation was the first to reach scan times below 20 seconds for a scan of a whole body part. The broad fan beam is able to capture a complete patient and irradiate the detector arc so that the translation was dispensable and only the rotation was required. Also a fourth generation was introduced using a closed detector ring with only the tube rotating but nowadays the third generation became prevalent [16].

![Figure 2.1.: Basic concepts of the four different CT generations](image)
In this chapter the basic components of a CT system like x-ray tube, filter, and detector and their functionality are described. The chapter also provides an overview of the fundamental physics of x-ray generation and interaction with matter, as well as the principles of image reconstruction. However, only content and topics directly relevant for CT are elaborated. For further studies it is referred, among others, to the text books [6], [8], [16] and [22].

2.1. CT Fundamentals

2.1.1. Basic Structure

The gantry represents the dominant ring shape of a CT system. The rotating device comprises the essential components for image acquisition including x-ray tube and detector which are installed opposing each other. A schematic structure is depicted in Figure 2.2. [16, p. 46]

![Figure 2.2.: Basic setup of a CT system. X-ray source and detector are opposing each other, a bowtie filter behind the tube protects the patient from unnecessary radiation. The components are installed on the gantry which is rotating around central measuring field.](image)

The object of interest is placed on an examination table in the middle of the measuring field. The diameter of the gantry opening is usually about 70-80 cm with a measuring field of 50-60 cm. In the gantry the detector and the tube are rotating around the patient with rotation times between 0.25 and 1.5 s around the object to acquire at least 180° of projection data needed to reconstruct the cross-sectional images.
2.1. CT Fundamentals

2.1.2. X-ray Physics

In 1895 Wilhelm Conrad Röntgen discovered in experiments with accelerated electrons a new kind of rays with the ability of penetrating optically opaque objects [26]. He named it x-rays and the discovery was awarded the first Nobel Prize in physics in 1901 [1]. X-rays are electromagnetic waves and emerge for instance when decelerating fast electrons within anode material. They are part of the electromagnetic spectrum occurring between gamma radiation and ultraviolet light and because there is no clear definition the intervals partially overlap (Figure 2.3). X-rays have a very short wavelength ranging roughly from $10^{-12}$ to $10^{-8}$ m with energies between 1 keV and 0.5 MeV. For medical diagnostics energies between 10 and 150 keV are common [6]. Also the terms of soft x-rays (low energy) and hard x-rays (high energy) are commonly used [8].

![Figure 2.3.: Spectrum of electromagnetic waves. X-ray spectrum is found between \(\gamma\)-rays and UV light.](image)

2.1.2.1. X-ray Generation

The basic process of x-ray production used in medical applications is deceleration of electrons in matter. Therefore electrons are emitted from a cathode in a vacuum tube and accelerated in an electric field with high voltage $U_a$ on an anode. The principle of x-ray generation is shown in Figure 2.4.

![Figure 2.4.: Principle of x-ray generation. Electrons are ejected by a cathode, accelerated on an anode and hit the target material and produce x-rays.](image)
Due to energy conservation the electron velocity $v$ and acquired kinetic energy is

$$E_{\text{kin}} = e \cdot U_a = \frac{1}{2} m_e v^2$$

(2.1)

with the elementary charge $e = 1.602 \cdot 10^{-19}$ As and electron mass $m_e = 9.109 \cdot 10^{-31}$ kg. The energy unit is called electron volts (eV); 1 eV is the energy an electron gains by acceleration in an electric potential of 1 V. This is also the unit of x-ray photon energy [6, p. 16].

By hitting the anode material, the electrons lose their kinetic energy and several processes take place. The first is the collision of the electron with orbital electrons of the atoms in the material which are raised to higher energy levels or ionized. When the excited, or another, electron falls back to the equilibrium state it emits the so called characteristic radiation which derives from the characteristic distances between the energy levels of an atom. The second interaction is the deceleration of electrons in the electric field of the atomic nuclei of the anode material. This also results in the emission of radiation, the so called bremsstrahlung [6, p. 21]. All other collisions and interactions lead to a transfer of the energy to lattice vibrations, heating up the anode. More than 99% of the kinetic energy of the electrons is converted this way and so cooling the anode is essential. Less than 1% of the available energy is converted into x-rays in energy ranges relevant for medical diagnostics [22, p. 119].

2.1.2.2. X-ray Spectrum

introducing words of chapter

Figure 2.5.: X-ray spectrum with bremsstrahlung and characteristic radiation for 140 keV. The attenuation at low energies is caused by intrinsic absorption and filters. Adapted from [22, p. 121]

Bremsstrahlung

When electrons hit the anode material they are decelerated and deflected by the electric field of atomic nuclei. In this process, the charged particles produce electromagnetic
waves, the so called bremsstrahlung. The deceleration of the electrons in the anode material takes place in multiple scattering and stepwise loss of their kinetic energy. Subsequently, a continuous spectrum arises. If an electron transfers its entire kinetic energy $eU_a$ into a single photon, this defines the maximum energy of an x-ray photon and its frequency $\nu$ by

$$eU_a = h\nu_{\text{max}} = h\frac{c}{\lambda_{\text{min}}} = E_{\text{max}}$$  \hfill (2.2)

with Planck’s constant $h \approx 4.135 \cdot 10^{-15}$ eVs, the speed of light $c \approx 2.998 \cdot 10^8$ m/s and the wavelength $\lambda_{\text{min}}$ in [m]. X-rays of every energy below $E_{\text{max}}$ can occur. A typical spectrum is shown in Figure 2.5. The spectral intensity of the bremsstrahlung shows a linear dependence on the energy (dashed line in spectrum) and is proportional to the atomic number $Z$ of the anode material, so the slope is

$$I(\nu) \propto Z(E_{\text{max}} - E)$$  \hfill (2.3)

For high energies of a realistic spectrum (continuous line) this relation is quite accurate. At lower energies it differs due to internal absorption. If the energy of the x-ray photon is low, it is reabsorbed by the anode material before escaping. Inherent absorption also reduces the intensity of the radiation if its emitted at very shallow angles (>80°), also called the heel effect. Otherwise, the distribution of the intensity is nearly independent of the direction of emission. The overall conversion efficiency of the kinetic energy to the energy of bremsstrahlung can be described by

$$\eta = kZU_a$$  \hfill (2.4)

with Kramer’s constant $k$ empirically determined to be $\sim 10^{-9} \text{ V}^{-1}$ (thus it shows a dependence to $Z$) [6].

**Characteristic Radiation**

In an x-ray spectrum the bremsstrahlung is superimposed by the characteristic line spectrum (Figure 2.5), which is generated by the interaction of the accelerated electrons with electrons on the inner shell of the anode material. If an electron of an inner shell (K, L..) is ejected by an accelerated electron exceeding the binding energy of the shell electron, the atom is ionized due to the loss. An electron of a higher shell fills the vacant position and emits a photon. Electrons of higher shells represent a state of higher potential energy, so in the example of a transition to the K shell, the emitted photon possesses the energy difference $E_n - E_1$ between the shells with the corresponding wavelength given by Moseley’s law [6, p. 21]

$$\lambda = \frac{hc}{E_n - E_1} = \frac{hc}{13.6 \text{ eV}(Z - 1)^2(1 - 1/n^2)}$$  \hfill (2.5)

with \(n = 1, 2, \ldots\) being the quantum number of the K, L.. shell and the atomic number $Z$. The explicit notation of these transitions is illustrated in Figure 2.6. Descents from
the L-, M-, N-shell to the K-shell are denoted \( K_\alpha, K_\beta, K_\gamma \) and from the M-, N-, O-shell to the L-shell \( L_\alpha, L_\beta, L_\gamma, \) etc. Due to the high energy difference between the inner shells, the emitted photon is an x-ray quantum (e.g. in tungsten \( K_\alpha \approx 58 \text{ keV} \)). These discrete energies create the sharp lines of the x-ray spectrum and are characteristic for the anode material.

![Simplified energy level transitions in tungsten. The denotation of the transitions is composed of the destination shell and its index which counts the number of transitioned shells. Adapted from [22, p. 122]](image_url)

### 2.1.3. X-ray Tube

The x-ray tube is an essential component of an x-ray imaging system. The tube voltage determines the maximum energy of the x-ray spectrum as well as the spectral distribution and thus image characteristics. The voltage is adjusted with respect to the object which is examined, i.e. its shape and material characteristics and the contrast ratio. A thoracic bone structure, for example, requires approximately half of the voltage an image of the chest would require to receive information behind the ribs [22, p. 300].

A schematic drawing of an x-ray tube is shown in Figure 2.7. Electrons are emitted from a cathode and accelerated on a rotating anode. The cathode is a filament which is heated directly to overcome the binding energy of the electrons in metal. The electron beam is formed by electron optics to provide a small focus on the anode. A cup shaped electrode, the so called Wehnelt cylinder, generates an electric field near the cathode so the beam can be controlled and is focused on a small spot on the anode. In CT, typical focus diameters of the tubes range between 0.5 and 1.2 mm [16, p. 50].

High atomic numbers for the anode material of an x-ray tube lead to more efficient x-ray generation. However, using Equation 2.4, even for a tungsten anode \( Z(W) = 74 \)
and an acceleration voltage of $U_a = 140\, \text{kV}$, the conversion efficiency would be less than $\eta = 0.01$ [22, p. 123]. This means, more than 99% of the kinetic energy is converted to heat. So material with a high melting point is equally important. Selecting the optimal material, the following criteria for quality $Q_{\text{mat}}$ must be fulfilled: large $Z$, high melting point temperature $\vartheta_{\text{max}}$ and high thermal conductivity $\lambda$, so

$$Q_{\text{mat}} = Z\vartheta_{\text{max}}\lambda$$

(2.6)

where $Q_{\text{mat}}$ has to be maximized [22, p. 123]. To further reduce the heat on the target material, rotating anodes are used. The focus is thereby spread on a focal line rather than being concentrated on one single spot. Typically, the speed is about 6000 rotations per minute [8, p. 24]. For rotating anodes, a little modification of Equation 2.6 (including the density $\rho$ and the specific heat $c$) provides better results [8, p. 27].

$$Q_{\text{mat,rot}} = Z\vartheta_{\text{max}}\sqrt{\lambda\rho c}$$

(2.7)

Tungsten fulfills these requirements best. Other target materials are used for special applications, e.g. molybdenum for mammography [22, p. 124].

### 2.1.4. Interaction with Matter

Due to their high energy and very short wavelength, x-rays have a material dependent capability of passing through objects. Still, interactions with matter like absorption and scattering decrease the number of detected photons. This attenuation is used in medical diagnostics to generate images of within the body as organs and bones. The attenuation of $N$ photons on a thin material layer with thickness $dx$ is defined by

$$dN = -\mu N\, dx$$

(2.8)
2. Computed Tomography

Figure 2.8.: N photons impinge on material with thickness dx. N + dN photons pass through with dN being negative.

with the attenuation coefficient \( \mu \) (Figure 2.8).

For an homogeneous object with thickness \( d \) and monochromatic radiation, the integration of Equation 2.8 leads to Lambert-Beer’s law [6, p. 33]

\[
N = N_0 \cdot e^{-\int_0^d \mu(x)dx} \rightarrow N = N_0 \cdot e^{-\mu d}
\]  
(2.9)

where \( N_0 \) is the number of incident photons. This equation only holds for a simplified model with a pencil beam, where scattered radiation is not taken into account. In general, the attenuation coefficient is given by [6, p. 33]

\[
\mu = \frac{\rho N_A}{A} \sigma_{\text{tot}} = n \cdot \sigma_{\text{tot}}
\]  
(2.10)

with the density \( \rho \), atomic number \( A \) of the material and the Avogadro constant \( N_A \). So the attenuation coefficient is given by the number of target atoms per unit volume \( n \) times the total cross section \( \sigma_{\text{tot}} \) of the photons for either scattering or absorption. With the attenuation of x-rays being proportional to the density \( \rho \) the mass attenuation coefficient \( \mu/\rho \) can be defined. In Figure 2.9, \( \mu/\rho \) over the energy is illustrated schematically for soft tissue.

The attenuation of x-rays passing through material is an addition of two main processes, scattering and absorption, which comprise the photoelectric effect, coherent and incoherent scattering as well as pair production. To produce an electron-positron pair, photon energies of at least \( h\nu = 1.022 \text{ MeV} \) are necessary. The pair production occurs only if the photon energy is equal or higher than the energy which, according to Einstein’s \( E = mc^2 \), is comprised in the sum of the rest masses of electron and positron, \( 2 \times 511 \text{ keV} \). Thus, for the diagnostic energy window of 25 – 150 keV, this effect has no relevance to the attenuation (see Figure 2.9). Therefore, the total linear attenuation coefficient can be summarized as

\[
\mu = \mu_{\text{photo}} + \mu_{\text{Compton}} + \mu_{\text{Rayleigh}}
\]  
(2.11)

with the attenuation coefficients of photoelectric effect \( \mu_{\text{photo}} \), Compton scattering \( \mu_{\text{Compton}} \) and Rayleigh scattering \( \mu_{\text{Rayleigh}} \) [22, p. 124].

Rayleigh Scattering

Rayleigh scattering occurs if the wavelength of the incident x-ray photon is large compared to the diameter of the scattering particle. In this case the photon is scattered coher-
2.1. CT Fundamentals

Figure 2.9: Mass attenuation coefficient of soft tissue as a function of energy. For energies below 100 keV the photoelectric effect is dominant, between 100 keV and 2 MeV it is the Compton effect and above 2 MeV pair production. The diagnostic energy window is highlighted in gray. Adapted from [6, p. 41]

ently, which means it does not change its wavelength but its direction (see Figure 2.10). Consequently there is no absorption or energy transfer. However, the deflection enlarges the total cross section,

\[ \sigma_{\text{coherent}} \propto \frac{Z^2}{E^2}, \]  

but with a squared dependence on the energy it decreases rapidly for energies above 10 keV [6, p. 131]. Inserting \( \sigma_{\text{coherent}} \) into Equation 2.10 this yields for the mass attenuation

\[ \frac{\mu_{\text{Rayleigh}}}{\rho} \propto \frac{Z^2}{A} \frac{1}{E^2}. \]  

Photoelectric Effect

For "his discovery of the law of the photoelectric effect" Albert Einstein was awarded a Nobel Prize in 1921 [2]. An x-ray photon with energy \( E \) is completely absorbed by an bound electron if the binding energy \( E_b \) is smaller than \( E \). The electron is ejected from the atom possessing the energy difference of the incident photon and the energy it was bound to the atom (cf. Figure 2.11). The resulting vacancy is filled by an electron of a higher but lower energetic shell emitting characteristic radiation as already described
in Subsection 2.1.2.2. The subsequent created vacancies are filled in the same way. If the transition takes place in inner shells of nuclei with high atomic number, the emitted energy is high enough to be in the range of x-rays. However, the released energy also has the ability to kick out another electron from the same atom. The so called Auger electron is not accompanied by radiation so the process is referred to as internal conversion. In elements with high atomic numbers the probability of creating an Auger electron is nearly zero, in material with low atomic numbers almost one.

The absorption of the photoelectric effect is dependent on the energy $E_{\text{in}}$ of the incident x-rays and the atomic number $Z$ of the material. The absorption coefficient $\mu$ can
therefore be written as [6, p. 36]

\[ \mu_{\text{photo}} \propto \frac{\rho Z^4}{A(h\nu)^3} \]  

(2.14)

where \( A \) is the atomic weight of the material. With \( A \) being linear dependent on \( Z \), the mass attenuation coefficient \( \mu/\rho \) is dependent on [6, p. 36]

\[ \frac{\mu_{\text{photo}}}{\rho} \propto \frac{Z^3}{(h\nu)^3} \]  

(2.15)

Figure 2.12 depicts the mass attenuation for the photoelectric effect of xenon as a function of the photon energy in a log-log-graph. The steep decrease is interrupted by characteristic absorption edges at photon energies corresponding to the binding energies of the electrons. X-ray photons with energies slightly higher than the binding energy have an increased probability (up to 80%) that photoelectric absorption takes place.

Figure 2.12.: Mass absorption coefficient \( \mu_{\text{photo}}/\rho \) of xenon as a function of energy \( h\nu \). Adapted from [22, p. 127].

**Compton Scattering**

In 1927, Arthur Holly Compton received the Nobel Prize for discovering the nature of incoherent scattering named after him, the Compton scattering [3]. Whereas in the photoelectric effect the incident photons interact with bound electrons of inner shells, the Compton effect describes the interaction of photons with electrons of outer shells. The binding energy of the electrons is very small compared to the energy of the incoming
2. Computed Tomography

photons, so these electrons are considered as quasi-free. If an x-ray photon collides with a quasi-free electron it transfers energy as well as momentum to it so the electron is kicked out of the shell. The electron then possesses the energy $E_e$ under the deflection angle $\theta$ (see Figure 2.13). The x-ray photon also undergoes a deflection of the angle $\phi$ and now has a reduced energy $E' = h\nu'$. Due to energy and momentum conservation the energy of the scattered photon can be calculated by the difference in wavelengths

$$\Delta \lambda = \lambda - \lambda' = \frac{h}{m_0 c} (1 - \cos \phi). \tag{2.16}$$

With the rest mass $m_0$ of the electron, the constant $h/m_0 c = 2.43 \cdot 10^{-12}$ m is referred to as the Compton wavelength. The increase in wavelength is thereby independent of the incident photon energy. Equation 2.16 says that there is no energy transfer in forward scattering, the maximum energy transfer occurs for backscattering at $\phi = 180^\circ$. However, even in this case the x-ray photon retains at least two thirds of its initial energy [6, p. 38].

![Figure 2.13: Schematic process of the Compton scattering. Incident x-ray photon ejects electron, transferring some of its energy to it and undergoes deflection. Adapted from [22, p. 129]](image)

The Klein-Nishina formula gives the cross-section of the Compton interaction per unit solid angle and per electron scattered at angle $\phi$ in dependence of the energy [22, p. 129]

$$\frac{d\sigma_{\text{Compton}}^e}{d\Omega} = \frac{r_0^2}{2} \left( \frac{h\nu'}{h\nu} \right)^2 \left( \frac{h\nu'}{h\nu} + \frac{h\nu}{h\nu'} - \sin^2 \phi \right) \tag{2.17}$$

with the classical electron radius $r_0 = e^2/m_0 c^2 = 2.82 \cdot 10^{-15}$ m. In the process of Compton scattering the energy of the incident photon is split between the recoil electron and the scattered photon, so the fraction of transferred energy from the photon to the electron...
can be described in a total cross section
\[ \sigma_{\text{transfer}}^e = \int \frac{d\sigma_{\text{Compton}}^e}{d\Omega} \frac{E}{\hbar \nu} d\Omega. \]  
(2.18)

Inserting Equation 2.18 in Equation 2.10 allows the derivation of the dependencies of the mass attenuation coefficient for Compton scattering
\[ \frac{\mu_{\text{Compton}}}{\rho} \propto \frac{Z}{A} \sigma_{\text{transfer}}^e. \]  
(2.19)

For the approximation of \( Z/A \approx 0.5 \) the attenuation coefficient \( \mu_{\text{Compton}} \) is nearly independent of \( Z \) [22, p. 130].

### 2.1.5. Filter

A CT system possesses several collimators and filters to shape and modify the emitted x-ray spectrum. The first aperture is directly mounted at the x-ray tube near the focus to define the opening angle of the fan beam. The second collimator is adjustable to vary and define the beam exactly.

The filtering of the spectrum is divided in several steps. The tube already absorbs internally, e.g. when x-rays are absorbed before leaving the anode material (see Subsection 2.1.2.2). This attenuation is in the magnitude of a 3 mm aluminum layer. Additionally, flat and formed filters are used for pre-filtration. Flat filters usually consist of aluminum and shift the x-ray spectrum towards higher energies to reduce the amount of soft x-rays harming the patients surface (cf. Figure 2.5). Due to their low energies soft x-rays are absorbed before passing the object and contribute therefore mainly to patient dose but not to the imaging signal. Formed filters, so called bow-tie filters, attenuate the radiation less in the center of the beam and more in the periphery. This protects the periphery of the object from needless radiation exposition as well as yields to a uniform signal across an object. Figure 2.14 illustrates the basic process. [16, 51ff.]

### 2.1.6. CT Detector

The purpose of medical imaging x-ray detectors is to absorb the incident x-rays efficiently and to convert them into a geometry-conserving image signal [22, p. 334]. In this section, a conventional x-ray detector is described. The interaction principles of x-ray photons and matter have already been explained in Subsection 2.1.4, so no additional effects have to be introduced to describe the interaction between x-rays and detector material. As a consequence, x-ray photons are not measured directly but indirectly via their interaction products, e.g. a photoelectric electron. The detection efficiency is defined mainly by the geometric efficiency (also called fill factor) and the quantum efficiency. The fill factor describes the ratio of the x-ray sensitive area of the detector to its total area. The quantum efficiency refers to the ratio of photons being absorbed and contributing to the signal to the total amount of incident photons. [6, p. 48]
2. Computed Tomography

Figure 2.14.: Illustration of the different filter types.

Energy integrating detectors are the most widely used detectors in CT systems today. They are based on an indirect conversion process which consists of two steps (ct. Figure 3.1). The x-rays are absorbed by a scintillator material creating a fast photoelectron. While losing its energy, the electron creates scintillation light in the visible range. This light is collected by a photodiode and converted into electric charge which is proportional to the intensity of the incident x-ray beam. [22, p. 336]

Figure 2.15.: Concept of a scintillator detector. Single channels are separated by anti-scatter lamella. The scintillator converts incident x-rays to visible light which is detected by a photodiode.

A typical scintillator material for flat detectors is gadolinium oxysulfide (Gd₂O₂S) [16, p. 54]. The choice of the material depends on the desired quantum efficiency which is provided by the mass attenuation coefficient. At a 80 keV x-ray spectrum, CsI with a
thickness of 0.6 mm yields an absorption efficiency of >70%, 1.4 mm of Gd$_2$O$_2$S up to 95%.

Anti scatter grids are attached to the detector elements to suppress undesired deflected radiation. The lamella are directed towards the focus to avoid the photons that are not traveling on the line connecting focus and detector. Without a grid the noise would be higher and therefore the image quality reduced. However, to effectively block oblique entrancing x-ray photons lamella with a thickness of at least 0.1 mm are required. The subsequent lower geometric efficiency also reduces the spatial resolution [6, p. 55].

For the photodiodes, detecting the light, amorphous silicon shows several favorable properties. The semiconductor characteristics are suitable for electrical components like photodiodes. Also the material allows large-format deposition enabling the construction of large active matrices. The high radiation resistance makes amorphous silicon suitable for medical applications with x-rays. When the light photons hit the photodiode, they are absorbed and converted to an electric charge proportional to the energy of the x-ray. During exposure the photodiode acts as a capacitor and integrates the incident x-ray source spectrum $S(E)$ over the energy, so that [12]

$$I \propto \int S(E) \cdot D(E) \, dE$$  \hspace{1cm} (2.20)

The detector responsivity $D(E)$ is thereby almost linear proportional to the energy, which leads to an energy-dependent weighting of the signal in Equation 2.20

$$I \propto \int S(E) \cdot E \, dE$$  \hspace{1cm} (2.21)

The read-out process is initiated by the TFT, switching the charge to external electronics as a signal. The read-out is performed for all pixels of a row simultaneously, measuring the charge and amplifying the signal by an Application-Specific Integrated Circuits (ASIC). The signal is now available for further image processing and reconstruction. [22, 335 ff.]

2.2. Image Reconstruction

In this section the mathematical fundamentals of image reconstruction are discussed. The topic would exceed the scope of the thesis, so it is limited to the algorithms used in CT. This section is largely based on [16, 263 ff.], [6, 151 ff.] and [8, 131 ff.] which are also recommended for further investigation.

2.2.1. Reconstruction Algorithms

A possible way to classify the different reconstructions of tomographic image is the division in analytic reconstruction algorithm, algebraic methods and statistic techniques.

The analytic method understands the object as a function $f(x, y)$ and the projection data as $p(\vartheta, \xi)$ with the projection length $\xi$ under the angle $\vartheta$, see Figure 2.16. The reconstruction problem is therefore the solution of an integral equation by inverting it exactly or
approximated by an inherent discretization of the measured data. The advantages of the analytic reconstruction algorithm is its ruggedness and high performance compared to other methods.

In contrast, the algebraic method is based on the discretization of the measured data. An object is understood consisting of grey values \((f)\) and the projections \(p\) (see Figure 2.16) are the sum of values along the projection line, so line integrals. For the entire set of measured values it gives a system of linear equations \(p = M \cdot f\), where \(M\) describes the process of measurement including the weights of \(f\) for \(p\). To reconstruct the image, the equation has to be solved. Due to uncertainties, errors and noise it is not possible to calculate the inverse \(M^{-1}\) so the equations have to be solved iterative. This is extremely time intensive and is therefore not applicable in clinical routines.

The third class of reconstruction algorithms is also of iterative nature. In contrast to algebraic processes the statistic reconstruction is modeling the probability \(P_f(p)\) of detecting values. The unknown parameters \(f\) are chosen in a way that \(P_f(p)\) is maximized. This concept provides the best use of dose as well as the lowest noise within same image quality of all methods [16, p. 265]. But, analogous to the algebraic algorithms, the computational effort for this reconstruction is orders higher than for the analytic to be implemented in clinical applications.

In the following, the concept of analytic image reconstruction is introduced.

![Image](image.png)

Figure 2.16.: Definition of the geometry for basic image reconstruction with the object \(f(x, y)\) and its projection \(p(\theta, \xi)\)

### 2.2.2. Analytic Reconstruction

In clinical CT systems the filtered backprojection is the most common method used for image reconstruction. The principle can be demonstrated with the reconstruction of 2D parallel beam data. Although no clinical scanner is using parallel beam geometry, fan and cone beam reconstruction can be derived by it.
2.2. Image Reconstruction

Definition of the 2D Parallel Projection

The object function is defined as \( f(x, y) \). The object is inside the rotation center, outside of this measuring field \( f(x, y) \) is zero. In parallel geometry the beam is described by its angle \( \vartheta \) and the distance \( \xi \) to the origin of the coordinate system (cf. Figure 2.16) which gives the line \( x \cos \vartheta + y \sin \vartheta = \xi \). Every measured value corresponds to the integral through the object \( f(x, y) \) along that beam:

\[
p(\vartheta, \xi) = p_\vartheta(\xi) = \int \delta(x \cos \vartheta + y \sin \vartheta - \xi) \, dx \, dy \tag{2.22}
\]

with the Delta Dirac function \( \delta \) and the projections \( p \) of the object \( f \). This transformation of \( f \) in \( p \) is called the Radon transform, with its transformation operator \( R \) and a projection angle \( \vartheta \) which, to simplify matters, is fixed. Equation 2.22 can also be written as

\[
p = R\{f\}. \tag{2.23}
\]

Reconstruction of Parallel Data

As seen in Equation 2.23, the inverse Radon transform \( R^{-1} \) is needed for calculating the original object which is not feasible directly. Therefore, the Filtered Backprojection (FBP) is introduced, as it is the most common used algorithm.

First, the Fourier transform (\( \mathcal{F} \)) of a function \( g(x) \) is defined as

\[
\mathcal{F}\{g\} = G(u) = \int_{-\infty}^{\infty} dx \, g(x) e^{-2\pi iux} \tag{2.24}
\]

with its inverse transform

\[
\mathcal{F}^{-1}\{G\} = g(x) = \int_{-\infty}^{\infty} du \, G(u) e^{2\pi iux}. \tag{2.25}
\]

Applying the one-dimensional Fourier transform on Equation 2.22 the projection \( p_\vartheta(\xi) \) in respect of the distance \( \xi \) gives

\[
\mathcal{F}_1\{p_\vartheta\} = P_\vartheta(u) = \int d\xi \, p_\vartheta(\xi) e^{-2\pi iux} = \int \delta(x \cos \vartheta + y \sin \vartheta - \xi) \, dx \, dy \, f(x, y) e^{-2\pi i(x \cos \vartheta + y \sin \vartheta)} \tag{2.26}
\]

Comparing \( P \) now with the two-dimensional Fourier transform on \( f(x, y) \)

\[
\mathcal{F}_2\{f\} = F(u_x, u_y) = \int dx \, dy \, f(x, y) e^{-2\pi i(u_x x + u_y y)} \tag{2.27}
\]

and changing the coordinates from Cartesian to polar coordinates with \( (u_x, u_y) = (u \cos \vartheta, u \sin \vartheta) \), it leads to the Fourier-Slice-Theorem

\[
F(u \cos \vartheta, u \sin \vartheta) = P_\vartheta(u) \tag{2.28}
\]
This means, \( P_\vartheta(u) \) describes the values of \( F(u_x, u_y) \) on a line at an angle \( \vartheta \).

Obviously, Equation 2.28 can be used directly to calculate the object function \( f(x, y) \) by applying the inverse two-dimensional Fourier transform \( \mathcal{F}^{-1}_2 \) on \( F(u \cos \vartheta, u \sin \vartheta) \). This is

\[
\mathcal{F}^{-1}_2 \{ F \} = f(x, y) = \int_0^\pi \int_{-\infty}^{\infty} \mathrm{d} \vartheta \int_{-\infty}^{\infty} \mathrm{d} u \ P_\vartheta(u) e^{2\pi i u \xi} \bigg|_{\xi = x \cos \vartheta + y \sin \vartheta} (2.29)
\]

To further simplify Equation 2.29, the convolution theorem is introduced. It says that the Fourier transform of a convolution of two functions \( g_1 \) and \( g_2 \)

\[
g_1(x) \ast g_2(x) = \int \mathrm{d}x' \ g_1(x')g_2(x-x')
\]

(2.30)
can also be implemented by a multiplication of the Fourier transform of each function \( G_1 \) and \( G_2 \).

\[
\mathcal{F} \{ g_1 \ast g_2 \} = \mathcal{F} \{ g_1 \} \cdot \mathcal{F} \{ g_2 \} = G_1(u) \cdot G_2(u)
\]

(2.31)
The two factors in Equation 2.29 can now be directly identified as the Ramp-Kernel and the Fourier transform of the object function. The kernel is defined as

\[
K_e(u) = |u| e^{-|u|}. \quad (2.32)
\]

Since \( |u| \) is not a square integrable function a convergence-generating regular sequence of functions must be applied to obtain the kernel \( k(\xi) \) [6]. Therefore the inverse Fourier transform is

\[
k_e(\xi) = \frac{e^2 - (2\pi \xi)^2}{(e^2 + (2\pi \xi)^2)^2}.
\]

(2.33)

Finally, for the limit of \( \epsilon \to 0 \) the kernel converges to the function

\[
k(\xi) = \lim_{\epsilon \to 0} k_e(\xi) = -\frac{1}{2\pi^2 \xi^2}
\]

(2.34)
which leads to the filtered backprojection formula

\[
    f(x, y) = \int_0^\pi d\vartheta \, P_\vartheta(\xi) \ast k(\xi) \bigg|_{\xi = x \cos \vartheta + y \sin \vartheta}.
\]  

(2.35)

The inversion formula says that the projection data has to be convoluted with a reconstruction kernel. This convolution is then integrated along the sinusoidal line \( \xi \) for all angles \( \vartheta \) within an interval of \( 180^\circ \). The result is the pixel value at \( (x, y) \) of the original object. The complete reconstruction process is summarized in Figure 2.18.

![Figure 2.18: Schematic presentation of the filtered backprojection.](image)

The second step in the reconstruction, the integration, is equal to the "backsmearing" of the single, convoluted projections along the initial beam direction. The values of every projection are added on each pixel which is involved to obtain an image of the original object. Figure 2.19 shows a visualization of the backprojection process.

![Figure 2.19: Schematic presentation of the backprojection process. Each projection of the dot is backprojected, or smeared back per section. The addition of the backprojections results in a reconstruction of the dot.](image)
Reconstruction Kernel

The reconstruction kernel was above defined as

\[
K_e(u) = |u| e^{-|u|}, \quad k_e(\xi) = \frac{\epsilon^2 - (2\pi \xi)^2}{(\epsilon^2 + (2\pi \xi)^2)^2} \quad \epsilon \rightarrow 0 \rightarrow \frac{1}{2\pi^2 \xi^2}
\]  

\(2.36\)

Figure 2.20.: Reconstruction kernel \(k_e(\xi)\) and its Fourier transform \(K_e(u)\) for decreasing \(\epsilon\).

Figure 2.20 shows \(k_e(\xi)\) and its Fourier transform \(K_e(u)\) for decreasing \(\epsilon\). The reconstruction kernel is also referred as a filter because it basically is a high-pass filter and allows to influence the characteristics of the image. Applying a low pass filter, a so called soft or smooth kernel, softens the image by reducing noise and spatial resolution, a high pass filter, also called sharp kernel, enhances the edges by increasing resolution and noise (see Figure 2.21).

2.3. Image Appearance

2.3.1. Hounsfield Scale

Attenuation values from Equation 2.9 in CT are usually represented as gray values. Due to different settings in image acquisition, a direct comparison of CT images is not possible. Godfrey Hounsfield introduced an approach to map attenuation values \(\mu\) onto a dimensionless scale based on the value of water \(\mu_{\text{water}}\). An arbitrary tissue with \(\mu_n\) is defined as

\[
\text{CT-value} = \left( \frac{\mu_n - \mu_{\text{water}}}{\mu_{\text{water}}} \right) \cdot 1000 \text{ HU}, \quad (2.37)
\]
2.3. Image Appearance

Figure 2.21.: Schematic effects of different convolution kernels on a projection. Adapted from [16]

measured in Hounsfield unit (HU). On this scale CT value 0 is assigned to water, air with approximately no absorption has a value of -1000 HU. Therefore, a water and air calibration is made for each image so that they mark the fixpoints of the scale [16, p. 32]. Bone has a rather large absorption coefficient yielding to values up to 2000 HU and higher. In general, lung and fat have negative values, organs and muscles positive. The typical distribution of CT values is illustrated in as depicted in Figure 2.22. The scale is not limited to a maximum value but for medical purposes the values usually range from -1024 HU to +3071 HU which gives 4096 different grey values. Since the attenuation values of most organs are similar to water, careful distinction is required.

Windowing describes a gray-level mapping or contrast enhancement, by modifying the CT image gray-scale. This changes the appearance of the image to highlight particular structures. It is defined from C - W/2 to C + W/2, where W is the window width and C the window center. The window width is the range of CT numbers the image contains and varies the brightness of the image. A wide window is best used for areas with high difference in attenuation values, a narrow window can enhance the soft tissue contrast if the examining area has similar attenuation values. The window center is the midpoint of the range of CT numbers that are displayed and adjusts the contrast. Lowering the window center brightens the image and vice versa.

2.3.2. Image Noise

The measurement of CT values is based on statistical processes, so every measured value is afflicted by an uncertainty. In an ideal case, the errors should only be caused by quan-
2. Computed Tomography

Figure 2.22.: Extract of the Hounsfield scale

tum noise of x-ray generation and detection. For modern systems, the electronic noise is small compared to quantum noise [16, p. 106].

Noise-related errors in the measurement affect the reconstructed CT images, where it is noticeable as pixel noise. The noise, $\sigma$, is the standard deviation of the values of $N$ pixels with the pixel values $x_i$ in a certain homogeneous area, Region of Interest (ROI), regarding their mean $\mu$:

$$\sigma^2 = \frac{1}{N-1} \sum_{i=1}^{N} (x_i - \mu)^2$$  \hspace{1cm} (2.38)

where $\sigma^2$ denotes the variance. These measurements are usually performed with a water phantom. The noise $\sigma$ is increasing if less x-ray quanta are detected, so at high attenuation $k/I$ by highly absorbing objects, at low currents per scan time (mAs-product) and at small slice thicknesses $S$ (mm). The noise is thereby not in linear dependence of these factors but varies with the square root

$$\sigma = f_A \sqrt{\frac{k/I}{\varepsilon \cdot Q \cdot S}}$$  \hspace{1cm} (2.39)

with the total efficiency of the system $\varepsilon$ and the influence of the reconstruction algorithm $f_A$ [16, p. 106]. Sharp algorithms with high resolution increase the noise whereas smooth, contrast enhancing algorithms reduce the noise. As for the relation of the mAs-product - and therefore the dose $D$ - and noise, Equation 2.39 can be simplified to

$$\sigma \propto \sqrt{\frac{1}{D}}$$  \hspace{1cm} (2.40)

This means that to reduce the noise by half the dose has to be increased by a factor of 4 [16, p. 154]. For a more direct comparison of dose and noise, Equation 2.40 can be rewritten as

$$\sigma^2 \propto \frac{1}{D}$$  \hspace{1cm} (2.41)

which gives a linear correlation between dose $D$ and variance $\sigma^2$. This relation is used for the evaluation later.
2.3.3. Modulation Transfer Function

For the quantitative description of resolution capacity and thus image quality in CT the Modulation Transfer Function (MTF) has proven useful [6, p. 412]. This function is used as functions of spatial frequency and describes how close two neighboring objects (lines) can get before they can no longer be distinguished. So the unit for spatial resolution is \([\text{lp/cm}]\) (line pairs per cm).

The derivation, as described in [22, 216 f.], is based on a simple, one dimensional model, where the input signal \(q_{\text{in}}(x)\) is changed by involving with the system \(S\), resulting in the output signal \(q_{\text{out}}(x)\) (see Figure 2.23).

![Figure 2.23.: Model for input and output relation](image)

\[ q_{\text{out}}(x) = S(q_{\text{in}}(x)) \] \hspace{1cm} (2.42)

The system can be characterized by its response to a peak-shaped input function

\[ \text{PSF}(x - x_0) = S(\delta(x - x_0)) \] \hspace{1cm} (2.43)

with the Dirac delta function

\[ \delta = \begin{cases} 
0, & \text{for } x - x_0 \neq 0 \\
\infty, & \text{for } x - x_0 = 0
\end{cases} \quad \text{and} \quad \int \delta(x) \, dx = 1. \]

where Point Spread Function (PSF) refers to one-dimensional cases. Knowing the PSF of a system allows to calculate the output signal as

\[ q_{\text{out}}(x) = \int q_{\text{in}}(x_0) \, \text{PSF}(x - x_0) \, dx_0 = q_{\text{in}}(x) \ast \text{LSF}(x) \] \hspace{1cm} (2.44)

using Equation 2.30. Now applying the Fourier transform, as described in Equation 2.24,

\[ Q_{\text{out}}(u) = Q_{\text{in}}(u) \cdot \text{MTF}(u) \] \hspace{1cm} (2.45)

defines the MTF as the Fourier transform of the PSF.

For CT systems, the MTF is calculated by measuring e.g. a thin wire which is representing a point in a slice and determines therefore the PSF. Applying the Fourier transform leads to the system MTF.
2. Computed Tomography

A CT imaging process consists of a series of different systems which are connected to each other. Therefore, the complete MTF\textsubscript{system} can be decomposed in its individual systems, so it can be written as the product of the two main imaging components

\[ \text{MTF}_{\text{system}}(u) = \text{MTF}_{\text{imaging hardware}}(u) \cdot \text{MTF}_{\text{imaging software}}(u). \] (2.46)

Concerning the hardware part of the imaging process, two components, namely the x-ray tube and the detector, play an important role. The limiting aspects of these components are the focal spot size and the spatial discretization of the detector [6, p. 412]. Therefore, the hardware MTF can be divided into

\[ \text{MTF}_{\text{imaging hardware}}(u) = \text{MTF}_{\text{x-ray tube}}(u) \cdot \text{MTF}_{\text{sampling}}(u). \] (2.47)

As for the MTF of the focus size, the focus size \( F \) is spatially extended and the detector is assumed as ideally punctiform, therefore the detector does not contribute to the first step. If a thin wire is in the center between detector and focus, the detected signal is a PSF with a rectangular shape and the width \( b_F \). The corresponding MTF is a \( |\sin u/u| \) function. For a punctiform focus and a extended detector size \( D \) the rectangular function has the width \( b_D \), vice versa. Inserted in Equation 2.46, this is

\[ \text{MTF}_{\text{imaging hardware}}(u) = \frac{\sin(\pi b_F u)}{\pi b_F u} \cdot \frac{\sin(\pi b_D u)}{\pi b_D u}. \] (2.48)

This shows, that the MTF\textsubscript{imaging hardware}(\( u \)) is better, the smaller \( b_F \) and \( b_D \) are. If the object of investigation is positioned exactly in the center, \( b_F = 0.5F \) and \( b_D = 0.5D \), so, e.g., for a focus and detector width of 1 mm, a resolution of 0.5 mm can be achieved.

The limitations of resolution of the imaging software are mainly given by inaccuracies in the interpolation and the kind of the reconstruction kernel, as described in Subsection 2.2.2. So the MTF of the software is divided into

\[ \text{MTF}_{\text{imaging software}}(u) = \text{MTF}_{\text{interpolation}}(u) \cdot \text{MTF}_{\text{reconstruction kernel}}(u). \] (2.49)
Photon Counting Detectors (PCD) applied for x-ray computed tomography provide several clinical benefits. Unlike in energy integrating detectors, PCDs are direct converters with the ability to detect single x-ray photons and therefore provide energy discriminating capabilities, the potential of dose reduction and the reduction of image noise [33]. This chapter focuses on the characteristics important for CT and is largely based on [33] and [29].

3. Detection Mechanism

In this section the basic architecture of PCD and the detection mechanism are outlined. Figure 3.1. Semiconductor materials with high atomic number Z to absorb x-rays effectively. A semiconductor sensor absorbs the x-rays, the signal is detected by the pixelated anodes and processed by read-out electronics.

![Figure 3.1: Schematic structure of a PCD. A macropixel, here defined by the collimator width, is divided into subpixel which are connected to the read-out electronics.](image)

Signal Generation

Due to its high atomic number Z, cadmium (zinc) telluride Cd(Zn)Te is chosen as sensor material absorbing x-rays in the CT-typical range of 20-140 keV effectively [33]. When the photons impinge on the sensor they interact with the material mainly via photoelectric effect or Compton scattering (cf. Subsection 2.1.4). In both effects an atom is ionized...
3. Photon Counting Detectors for CT

and an electron ejected. This electron loses its energy by ionizing adjacent atoms and thereby creating subsequent mobile charge carriers (electron-hole-pairs) in the order of $10^{15} - 10^{17} \text{ cm}^{-3}$ [20, p. 56]. Due to a negative bias voltage with respect to the anode, an electric field causes the charge clouds to separate before they recombine and drift towards the electrodes (electrons to the anode, holes to the cathode). With moving charges in the vicinity of an electrode, a pulse signal is induced (as described by Shockley [27] and Ramo [25]). The height of the pulse, so the number of electron-hole-pairs, is thereby proportional to the absorbed energy of the incident x-ray photon. The integration of the signal current yields in the signal charge which is also proportional to the energy.

Detection and Signal Processing

To detect the incident x-rays the signal undergoes a preprocessing. Signal charges can be very small, i.e. $5 \cdot 10^{-17} \text{ C}$ for a 1 keV x-rays, so the signal has to be amplified. Afterwards, a pulse shaper improves the signal-to-noise ratio. Figure 3.2 shows the pulse shaping process. The preamplifier is configured as an integrator, converting the narrow pulse into a step impulse. A subsequent high-pass filter adds the desired decay which limits the pulse width. A low-pass filter (integrator) broadens the maximum of the pulse to a measurable time in the range of some $10^8 \text{ s}$. An analog-to-digital converter finally translates the continuously varying amplitudes to discrete steps.

![Figure 3.2: Components of a pulse shaping system. The signal current from the sensor is integrated to form a step decay with longer decay. The differentiator limits the pulse width and a subsequent integrator forms a smooth maximum. Adapted from [29]](image)

Energy Thresholds and Bins

PCDs can discriminate energy because of their ability to adjust multiple counter thresholds. An electric charge induces a pulse signal to an electrode and pulse height is compared to a adjusted threshold value. The induced signal is only registered as a count, if the height of the pulse exceeds the threshold value. Due to the pulse height being proportional to the incident x-ray photon a spectral discrimination of the signal is possible.

The second adjustment of pulse counting is also threshold based. Subtracting the counts between two adjacent energy thresholds, the resulting range is called energy bin and its
3.2. Advantages of PCDs

The advantages of PCDs in comparison to conventional energy-integrating CT detectors are summarized in the following.

- **Less Inherent Energy-Weighing** With the detector responsivity $D(E)$ being nearly constant over the energy, low x-rays are more equal weighted compared to energy-integrating detectors.

- **Intrinsic Spectral Sensitivity** The pulse height is correlated with the energy of the incident photons. Multiple counter thresholds allow to count the energies above certain values which results in an intrinsic energy discrimination.

- **Intrinsic High Resolution** The direct converter allows and requires, to avoid pulse pileup, going to smaller pixels by dividing them into subpixels. Smaller pixel lead to a higher spatial resolution.

- **Superb Low-Signal Performance** Photon counting detectors provide a high linearity in low signals. They are also able to exclude noise by adjusting a threshold right above the noise level, which increases the low signal performance.
3. Photon Counting Detectors for CT

3.3. Limitations and Spectral Distortions

In this section, the main physical effects which degrade the performance of the PCD are discussed. Afterwards, an assessment of the effects leads to the decision of reasonable parameters for detector.

Pulse Pileup

If the incidence of two photons in a single pixel is shorter than a pulse duration it is observed as one pulse at a higher energy than the energy of the initial two pulses, illustrated in Figure 3.4. The loss of counts and wrong registered energy results in a spectral distortion. In CT x-ray fluxes up to \(10^9\text{ s}^{-1}\text{mm}^{-2}\) \([18]\) are used so the requirements on the count rate linearity of PCDs are high.

![Figure 3.4.: Pulse pileup. If the interval of two incoming photons is shorter than the pulse duration, it can be registered as one count at higher energy. Adapted from [33]](image)

Charge Sharing

When an x-ray photon is absorbed by the PCD, it creates a charge cloud. The applied voltages let the charges drift towards their respective electrodes. Due to diffusion effects and the Coulomb force, the charge cloud broadens. If the charges reach the anode near a pixel boundary, some parts of the cloud may be detected by adjacent pixels (see Figure 3.5). This leads to a multiple count of a single cloud at lower energies than the original and
therefore to a distortion of the spectrum. This effect is called charge sharing and is dependent on the sensor material (which influences the mobility of charges), the pixel size, the applied voltage and the depth of interaction [33].

Figure 3.5.: Schematic process of charge sharing. If an incident photon is absorbed near a pixel boundary, the emerging charge cloud may be detected by adjacent pixels, too.

### K-Escape/ K-Fluorescence

When an x-ray photon interacts with the PCD via the photoelectric effect, as described in Subsection 2.1.4, a characteristic fluorescent x-ray photon is emitted. This photon is emitted in a random direction. It may therefore be absorbed in the pixel where the primary interaction took place, be detected in an adjacent pixel or leave the detector completely, as illustrated in Figure 3.6. In the first case, the photon interacts again with the detector material which may result in separate counts of the primary and secondary photon. In the latter two cases the detected energy of the primary photon is lower with respect to the energy the escaping characteristic photon inherits. Both cases lead to a spectral distortion.

### Compton Scattering

Another way of photon-matter-interaction is the Compton scattering, described in Subsection 2.1.4. Thereby the photon loses some energy and changes its direction. It can then be absorbed in the pixel of incidence, in adjacent pixels or leave the detector completely. In contrast to the discrete characteristic energy loss of photoelectric interaction, the energy loss of Compton scattering is dependent on the scattering angle and therefore continuous.

### Charge Trapping

The charge clouds also interact with the detector material. Electrons or holes can be captured by a trapping center and re-emitted delayed. In semiconductors trapping cen-
3. Photon Counting Detectors for CT

Figure 3.6.: Interactions between incident x-ray photons and detector. (a) Photon is absorbed and registered. (b) Photoelectric interaction leads to K-escape which is absorbed by the same pixel again resulting in a double-count. (c) K-escape photon absorbed in adjacent pixel, resulting in loss of energy and wrong count. (d) K-escape photon leaves detector completely resulting in a loss of energy.

ters arise as impurities or lattice defects. The delayed charges reduce the pulse height of the detected signal and lead to a deterioration of the detected pulse spectrum.

Design Considerations: Conflicts and Compromises

Some of the discussed effects above may be conflicting specifying the optimal setting for the PCD. Considerations for conceptional design of a detector system include e.g. [29]

- detector geometry
- quantum efficiency
- event rate
- readout circuits
- support structure, cabling, cooling
- cost

while these aspects cannot be optimized simultaneously.

Limits of Pulse Duration

The peaking time (pulse duration) is defined by pulse pileup and a sufficient amount of charge for the signal. In order to limit the pulse pileup, the peaking time should be as short as possible, so an upper limit is required to avoid a loss of counts. To collect the total signal of the charge clouds generated by x-ray photons it is necessary to extend the
peaking time. This defines the lower limit of the pulse duration to a time where spectral distortion is avoided by collecting just sufficient charge of the incident photon.

**Limits of Pixel Size**

The upper limit of the pixel size is defined by the spatial resolution of the reconstructed image and the amount of pulse pileup that can be tolerated. The larger the area of a pixel the higher is the probability of two signals impinging the pixel during one pulse. The limit of the lowest pixel size is determined by K-escape, charge sharing, and Compton scattering. These effects distort the recorded spectrum the more the smaller the size and to avoid them the lower limit of the pixel size has to be considerably larger than the size of the charge cloud and the reach of fluorescent photons.

The system design results of balancing the conflicting considerations [29]. Complex systems require compromises since the ideal solution is hardly practical. There is no single way to deal with this conflicting requirements so the effects relevant for the purpose outweigh the ideal solution.

### 3.4. Detector Response

The discussed effects that limit the resolution of PCDs can be seen in a detector response of a monochromatic x-ray beam with e.g. 100 keV. For an input quanta energy of 100 keV the probability distribution of the detected energy is given by Figure 3.7. Different effects can be seen in this response. Here, the peak at 100 keV is the photopeak, which means the incident 100 keV photon is detected as such. The peaks at about 75 and 25 keV can be explained by K-escape and K-reabsorption from neighboring pixels respectively. Below 25 keV charge sharing and noise build a floor.

![Figure 3.7: Modeled detector response of a PCD for mono-energetic x-rays with 100 keV.](image-url)
For a polychromatic energy spectrum with $E_{\text{max}} = 140$ keV, the detector response is shown in Figure 3.8.

Figure 3.8.: Incident x-ray spectrum and detector response for an energy spectrum with $E_{\text{max}} = 140$ keV.
4. Pseudo-Analytic Detector Model and Noisy Data Generator

The detector model which is used in this thesis was recently developed and published by Ken Taguchi et al. [34]. It is providing a realistic detector response function and accounting for effects such as spatio-energetic cross talk between pixels, interactions with PCD (see Subsection 2.1.4) and electronic noise. Each incident x-ray photon interacts with the photon counting detector material and creates charge clouds. If the interaction occurs near pixel boundaries, the signal can be detected by the two adjacent pixels (see Section 3.3). This means that PCD data is spatially and energetically correlated. The developed detector model uses a Poisson random number generator to create correlated counts. The modeled correlations are, for different pixels and energy thresholds, based on the assumptions of energy conservation and that no more than two pixels measure the signal of one photon. The model allows to generate projection data in different thresholds which can be reconstructed as measured CT data. It is also able to simulate the recorded x-ray spectra. In the following an overview of the detector model is given. For a more detailed description, see [34].

Figure 4.1.: Detector system model divided in different stages and probabilities to describe the energy input on a detector pixel. Adapted from [34]
4. Pseudo-Analytic Detector Model and Noisy Data Generator

The simulation, illustrated in Figure 4.1, is modeling the probability of the energy input of an x-ray photon on a detector pixel and the possible count in the adjacent pixel. To do so, the model is separated in different stages which all contribute with a certain probability to the output result.

As for the pixel correlation, the following assumptions were made. The pixel of interest (C) is in the center of a $3 \times 3$ pixel field, as shown in Figure 4.2(a), connected to eight neighboring pixels of which four pixels (X) share an edge (vertically or horizontally located) and the other four (D) share a corner (diagonal located). Each stage of the model is associated with a Probability Density Function (PDF) resulting in the recorded spectrum described by a Spectral Response Function (SRF).

![Figure 4.2:](image)

Figure 4.2: (a) Top view of a PCD pixel of interest (C) surrounded by neighboring pixels (X and D). (b) Side view of three adjacent pixels (X, C, X) with width $d_{pix}$. The charge cloud has a diameter $d_e$. The photon is completely absorbed if the cloud incidents at $d_e/2 \leq s \leq d_{pix} - d_e/2$, charge sharing occurs if incidence is at $0 \leq s < d_e/2$ and $d_{pix} - d_e/2 < s \leq d_{pix}$. Adapted from [34]

Combining the probabilities of the energy input with the probabilities of an additional count in neighboring pixels, the detector model is providing spatially and energetically correlated PCD data. The model can be implemented in a simulation software to generate CT projection data which can be further used for studies in different settings, reconstruction algorithms or image quality.

The advantage of the model lies in its very fast computational performance. Unlike Monte Carlo simulations, that are also available, the model reduces the processing time of an image simulation from several days to a few hours.
5. Validation of Detector Model

The detector model, which was introduced in chapter 4, has yet to be validated in terms of its accuracy and predictive power. Therefore, noise and its covariances across different threshold combinations are investigated and compared with the results of measurements with a real prototype CT scanner with PCD. To further use this model for reliable simulation, this step is inevitable.

5.1. Materials and Methods

5.1.1. Prototype Measurements

The prototype scanner, as introduced in [19], has the gantry of a commercially available clinical CT scanner, with a focus detector distance of 100 cm and a gantry opening diameter of 78 cm. The rotation time is limited to 0.5 and 1.0 s per rotation, the maximum adjustable values for the tube voltage are 140 kV and for the current 550 mA. A pre-filtration is made by a titanium filter of 0.9 mm thickness and additional 3.5 mm aluminum. The focal spot size is 0.8 mm. The photon counting detector consists of 30 modules 128 × 64 quadratic sub-pixels of 225 µm pitch which leads to a effective Field of View (FoV) of 27.5 cm. The sub-pixel size was designed to avoid pulse-pile up while reducing effects like K-escape or charge sharing as discussed in Section 3.3. Every sub-pixel has the ability of adjusting two individual energy threshold combinations. The thickness of the CdTe-based sensor, is 1.6 mm to provide an absorption capability comparable to conventional CT detectors and has a sensor bias-voltage of 1 kV. At the time of this study, the detector pixels could be read out in groups of 4 × 4 pixels, also called macro pixel. The anti-scatter grid mounted on top of the sensor is fitted to the macro-pixel geometry which leads to a 32 slice detector signal with an effective pixel size of 0.9 × 0.9 mm² active area and a pitch of 1.125 × 0.9 mm². Figure 5.1 illustrated the detector prototype.

For the measurements at the prototype scanner, a tube voltage of 140 kV, a current of 200 mA were and a rotation time of 1.0 s were chosen. The threshold combinations vary from 25, 35 and 45 keV as the lower energy threshold and 55, 65, 75 and 85 keV as the higher energy threshold. The pixel geometry of the macro pixel was used with 1152 views per rotation. One tomographic scan takes a few seconds. Afterwards, the scanned data undergo several corrections, i.e. beam hardening as well as a water scaling to adjust the data on the Hounsfield scale (see Subsection 2.3.1). A subsequent rebinning process transfers the data from fan beam geometry to parallel data which is required for
5. Validation of Detector Model

Figure 5.1.: Schematic structure of a PCD-prototype. The subpixel size is 225 µm and the macropixel size 1125 µm. The sensor thickness is 1.6 mm.

tomographic reconstruction. Image reconstruction algorithm is the Weighted Filtered Backprojection (WFBP) [31] with a kernel as typically used in clinical CT.

5.1.2. Simulation of Prototype Measurements

Detector model, as introduced in chapter 4, was implemented in a Siemens Healthcare internal simulation software package which allows performing detailed simulations of CT data [18]. The software is based on the simulation program DRASIM (Deterministic Radiological Simulation) [9]. It thereby simulates the attenuation in the filter, a phantom and the antiscatter grid for all x-rays between the focus and the detector pixel. The software calculations for the attenuation are based on the interaction of x-rays with matter, as described in Subsection 2.1.4. The phantom is geometrically defined by its volume geometry and material. In the last step, when the x-rays impinge the detector, the detector model is responding to the respective photon with a certain energy, as predefined in the model. The output data are in digital values. From this, images, spectra and dose values can be determined.

To directly compare the simulated output images, the same adjustments and sets of energy threshold combinations as for the measurements performed at the scanner prototype were chosen for the simulation.

5.2. Phantoms

5.2.1. Water Phantom for CT Prototype

The cylindrical phantom has a total diameter of 20 cm. In the center and 3 cm off the center two samples with a diameter of 2 cm can be inserted, here iodine-based contrast agents in the center and a water reference off the center. Figure 5.2 shows the phantom and the two inserts, the green tube is thereby filled with water and the clear tube with
iodine contrast agent. The phantom itself provides similar x-ray characteristics as water in clinically relevant photon energy ranges.

Figure 5.2.: Measurement phantoms. (a) Iodine and water inserts. (b) Inserted contrast agents. (c) View of backside with the attachment to fix it on the examination table.

5.2.2. Virtual Water Phantom for Simulations

The phantoms were modeled analogous to the measured phantoms, with an iodine contrast agent with a diameter of 2 cm in the center and water-like absorption material in a diameter of 20 cm.

Figure 5.3.: Simulation water phantom with iodine insert, with (a) axial and (b) longitudinal cross-section

5.3. Results

The simulated and measured projection data were reconstructed with the WFBP method and a medium smooth reconstruction kernel D40f. A slice thickness of 0.63 mm was
chosen, as this is the intrinsic slice width in the isocenter regarding the systems geometry and therefore avoiding smearing artifacts. The FoV of the image matrix was set to 220 mm. To compare the images, the attenuation values and noise were evaluated. Therefore, different ROIs were defined, as illustrated in Figure 5.4. The ROI for iodine is a circular area with radius 7 mm, the ROI of water is an annulus with inner radius of 60 mm and outer 75 mm to have a homogeneous area and avoid ring artifacts. The water ROI is chosen for image noise determination, due to its small size the iodine ROI is used for evaluation of attenuation values.

Figure 5.4.: Evaluated ROIs for iodine (center) and water (ring) in the (a) measurement, and (b) simulation.

**Absolute Noise Variance**

First, the water ROIs are evaluated. Therefore, the variance of the pixel values $\sigma^2$ is a good indicator for the incident counts. It is plotted for the energy threshold combinations 25 keV as lower and 55, 65, 75 and 85 keV as upper threshold. Figure 5.5(a) shows the absolute variances of the four threshold combinations for the measurement (red) and the simulation (blue): Thereby the threshold values of the measurements are 1.5 times higher than the simulations (Figure 5.5(b)). As already described in Subsection 2.3.2, the variance $\sigma^2$ is inverse proportional to the dose. This means, by measuring a variance 1.5 times higher than in the simulations compared to prototype scans, the dose in measurements is 1.5 times higher than simulated. This is taken carefully into account for all further dose evaluations.

After compensating the dose, Figure 5.5(b) indicates an additional offset in the upper energy threshold. Therefore, another set of simulations with the same lower energy thresholds as before, but with the higher energy thresholds being lower by 3 and 5 keV is added. Again, the variances $\sigma^2$ of new sets are compared to the measurements and confirm the observation of resizing the higher energy threshold. However, the difference of 3 and 5 keV also provide a high agreement. The validations for the other threshold combinations are attached to Section A.2.

To validate this difference in the upper energy threshold, several additional comparisons are made in the following including relative noises, covariances and HU values.
5.3. Results

Figure 5.5.: (a) Absolute noise variances in lower and higher threshold of measurement and simulation. (b) Simulation noise variance scaled by factor 1.5.

Figure 5.6.: Absolute noise variances in lower and higher threshold of measurement and simulation. Upper threshold of simulation additionally shifted by (a) 3 keV and (b) 5 keV.

Relative Noise Variance

As for a further criterion, the variances $\sigma^2$ of the pixel values in this area are normalized on the values of the lower energy threshold of each setting as a reference. The normalization is referred as an indicator of how well the energy thresholds vary in their correlation. The lower threshold provides thereby a good reference, as the values are more stable by holding the total counts. The results of simulation and measurement are compared. The setting of 25 keV as the lower and 55 - 85 keV in 10 keV steps are shown in Figure 5.7. The settings with the lower energy thresholds of 35 and 45 keV can be found in Section A.3. In Figure 5.7 the difference of the measurement and the simulation reoccurs. Taking in account the assumption of a shift in the upper energy threshold, the additional sets of simulations are evaluated. In Figure 5.8 higher energy threshold of the simulation is shifted down by 3 keV and 5 keV. This shows better conformity than the
5. Validation of Detector Model

![Figure 5.7: Relative noises variances of water of the simulation and measurement are compared for each energy threshold combination.](image)

Figure 5.7: Relative noises variances of water of the simulation and measurement are compared for each energy threshold combination.

direct comparison of the original settings, whereby the difference in 5 keV results in a higher agreement.

![Figure 5.8: Relative noises variances in water. Upper energy thresholds of the simulation are lowered by (a) 3 keV and (b) 5 keV.](image)

Figure 5.8: Relative noises variances in water. Upper energy thresholds of the simulation are lowered by (a) 3 keV and (b) 5 keV.

Covariances

Another indication of the correctness of the detector model is the correlation of the energy thresholds. This is done by comparing the covariances of noises. The covariance is a measure of the joint variability of two variables. In a one-dimensional case the covariance between two variables $x$ and $y$ is defined as [5, p. 96]

$$
\sigma_{xy} = \text{cov}(x, y) = \int \int (x - \mu_x)(y - \mu_y)f(x, y) \, dx \, dy
$$

$$
= E [(x - \mu_x)(y - \mu_y)]
$$

(5.1)
with the probability density function $f(x, y)$ of the variables. In two dimensions, this can be denoted as a covariance matrix with [5, p. 99]

$$
\sigma_x = E[(x - \mu_x)(x - \mu_x)^T] = \begin{pmatrix}
\text{var}(x_1) & \text{cov}(x_1, x_2) \\
\text{cov}(x_2, x_1) & \text{var}(x_2)
\end{pmatrix} = \begin{pmatrix}
\sigma_1^2 & \sigma_{12} \\
\sigma_{21} & \sigma_2^2
\end{pmatrix}
$$

(5.2)

where $x$ denotes a two dimensional vector. The diagonal elements of this matrix are the variances, the off-diagonal elements the covariances. The covariance is positive if the greater values of one variable, correspond with the greater values of the other variable and the same is given for the lower values. The covariance is negative in the opposite case, if the lower values of one variable correspond with the greater values of the other variable and vice versa. Here, the covariances of the two energy thresholds are compared.

The values of the covariance cannot be easily compared, because they are not normalized and depend on the magnitude of the variables. Therefore, the covariances are additionally normalized on the lower threshold, to achieve a comparability between the thresholds. The other threshold combination are attached to Section A.4.

Figure 5.9.: Normalized covariances for each threshold combination of measurement data (red), simulation data (blue) and shifted simulation data (green) by (a) 3 keV and (b) 5 keV.

The covariances provide good conformity for both variations in the upper threshold. The positive values show a linear dependence of the thresholds which was expected, as the lower threshold includes the values of the upper threshold.

CT Values of Iodine

The last investigated factor for the calibration in the upper threshold is the comparison of HU of the iodine (since water values are normalized). The HU of the images of the two thresholds are thereby plotted against each other for each set of threshold combinations, here 25 keV as lower, and 55 - 85 keV for the upper. Due to inaccuracies
5. Validation of Detector Model

in simulating the exact same concentration of iodine in the solution as in the sample used for the measurements, only the ratio of the CT-values is considered, absolute values can be neglected. The simulated CT-values should therefore lie along a line through the origin, as the ratio of the lower and upper threshold values should be the same for different concentrations of iodine in water. In Figure 5.10 the measured data (red circles) are compared to their respective simulation (blue cross). Also the simulations of 3 and 5 keV difference in the upper threshold are added. In this case, the 3 keV shift fits the measured data best, thus the 5 keV shift fits the measurement better than the original simulation. Threshold combinations for the lower thresholds 35 and 45 keV are attached to Section A.5.

Figure 5.10.: CT-values of iodine as measured, simulated and simulated with 3 and 5 keV differences respectively. Higher and lower thresholds plotted against each other for each set of threshold combination.
Conclusion

Several noise correlations of the images were investigated to provide a simulation in good agreement to measured data. As a result of this calibration, the dose values of the simulation needs to be scaled up by a factor of 1.5 to model the values correctly like in the measurements. Also a difference in the higher threshold of the simulation was discovered. Therefore, two variations of each 3 and 5 keV lower than the measured thresholds were investigated. The comparison of the covariances and the absolute noise values show an improvement for the variations, but do not differentiate much between 3 and 5 keV. The HU values fit better to the 3 keV shift whereas the relative noise values tend to align more for 5 keV lower. As the HUs underlie inaccuracies in the simulation, compared to the measurements respectively, as well as may have higher errors, due to the smaller evaluated ROIs (see Figure 5.4), the relative noise provides the decisive criterion. However, due to fact that the energy thresholds in the CT prototype are not adjustable as exactly as in the simulation, the offset is not measurable exactly. This calibration is only valid for the described CT prototype.

Altogether, simulations using two thresholds have to be adjusted in the upper threshold, reducing it by 5 keV and for the absolute noise $\sigma^2$ which is lower by a third - so a 1.5 times higher dose - compared to measurements has to be taken in account.

Note, that the adjustment of the upper threshold has been investigated for completeness only. The subsequent image study will be restricted to a lower threshold at 20 keV. This threshold provides the highest calcium contrast and the lowest image noise which is desirable for the detection of microcalcifications.
6. Mammography Simulation

In this simulation study it is investigated whether it is possible to provide clinically useful information of the breasts in whole body CT. As described in the introduction, a resolution of 100 µm is desired to ensure an identification of microcalcifications, their architecture and possible clusters. The advent of PCDs in whole body CT could provide the required high resolution. Therefore, a specially created synthetic thorax phantom including calcifications is created. This is used for simulations at different scanner and detector geometries to find the maximum resolution at adequate dose levels.

6.1. Materials and Methods

The detector model used for the simulations was already confirmed in chapter 5, implemented in the simulation software introduced in Subsection 5.1.2. The calibration results of the simulation are already taken into account. This model is now used to simulate CT images in geometries other than the prototype to investigate the resolution. As a reference, the images are compared to results of prototype simulations. The new detector geometries regarding the pixel size, focus diameter and intrinsic slice thickness, which is the slice thickness in isocenter, are listed in Table 6.1. The varied parameters pixel size, slice width and focus size are chosen because they contribute most to the limitation in resolution.

<table>
<thead>
<tr>
<th>Table 6.1.: Different simulation geometries (modes)</th>
</tr>
</thead>
<tbody>
<tr>
<td>mode</td>
</tr>
<tr>
<td>-----------------------</td>
</tr>
<tr>
<td>Mode 08 (M08)</td>
</tr>
<tr>
<td>Mode 03 (M03)</td>
</tr>
<tr>
<td>Mode 01 (M01)</td>
</tr>
<tr>
<td>Mode 01s (M01s)</td>
</tr>
</tbody>
</table>

The M08 is already realized in the existing prototype as a $4 \times 4$ read-out mode of 225 µm pixels. As described earlier, a macro pixel is assembled by $4 \times 4$ subpixels with a size of 225 µm and an active area of $900 \times 900$ µm which resembles the conventional energy integrating detector. M03, M01, and M01s are non existing geometries. The M03 mode with a focus diameter of 300 µm would be the only one which would be realistic to be realized in a whole-body CT scanner, so this one is especially interesting to investigate.
Scan settings are chosen from a protocol for thorax scans [32]. The tube voltage is 120 kV and the product of tube current with exposure time is 217 mAs. For the study it is also doubled (435 mAs) to reduce noise about a third and quadrupled (870 mAs) to halve noise. Additionally, an irrationally high dose value of 30000 mAs is chosen to demonstrate the resolution of the system by strongly reducing the noise. For the simulation a spiral scan with 2304 readings were adjusted per rotation, a 0.5 mm pitch and a rotation time of 0.5 s, also a threshold combination of 20 keV for the lower and 55 keV for the upper threshold.

### 6.2. Virtual Thorax Phantom for Simulation

For mammography purposes, a thorax phantom including breasts and calcifications is designed. The attenuation values of the respective materials are based on earlier studies on breast CT [15]. To simulate the whole body as accurately as possible, the thorax includes features like the spine, ribs, lungs and heart which are not explicitly investigated but contribute to the attenuation. The focus of investigation is set on the breast, in this case the left (right in Figure 6.1). The breast consists of a combination of glandular tissue and fat, in the center the amount of fat increases. Single glands are added as well as calcification spheres in different sizes. On the left side, the diameters of the calcification decrease from 1 mm down to 100 μm in order to easily access the resolution capability. In the three of the four glands also spheres with a diameter of 100 and one 200 μm calcification in the 6 mm gland.

![Figure 6.1.: Virtual thorax phantom (a) for simulation purposes including calcifications and glands with different sizes in the breasts (b)](image)
6.3. Results

Simulation geometries as described before in Table 6.1 are reconstructed and evaluated for a FoV of 40 mm using $1024 \times 1024$ pixel matrices. The image quality is compared in terms of noise ($\sigma^2$ and $\sigma$) and resolution. For the resolution, the image as well as a pixel line, drawn black in Figure 6.2, are compared. The noise of the tissue is evaluated in a circular area in the center of the phantom. The simulations are reconstructed with two different kernels. The first, $S80f$, is reconstructing the image with the maximum sharpness of the system, the second, $W80f$, provides the same sharpness for each image to compare them by noise. As discussed in Section 3.3, smaller pixel lead to an increased noise level due to effects like charge sharing and K-escape and will be the major factor of limitation in resolution.

![Figure 6.2: Glands calcifications with a black line marking the pixel-line plot and the circular ROI in the center to evaluate noise.](image_url)

6.3.1. Images with Maximum Resolution

The image reconstruction was performed with the WFBP and an $S80f$ kernel. $S80f$ is an artificial kernel, which optimizes its MTF so that the image is displayed up to the maximum possible sharpness of the system. In Figure 6.3 the image MTF for each geometry is plotted. Due to their similar geometry, $M03$ and $M01$ should provide a similar image sharpness and therefore similar noise levels. The images are grouped in the same dose values and compared regarding their resolution and noise. Therefore the gray values are adjusted with a fixed windowing for each dose value.
6. Mammography Simulation

Figure 6.3.: Image MTF of the S80f kernel for each geometry: M08, M03, M01 and M01s.

217 mAs

The images with the lowest chosen dose setting, 217 mAs, are compared. The adjusted window width is \( W = 3500 \text{ HU} \) with the center at \( C = 1300 \text{ HU} \). Figure 6.4 - Figure 6.7 displays the images for the modes M08, M03, M01 and M01s, as well as Table 6.2 lists the noise \((\sigma^2, \sigma)\) in the same order.

Table 6.2.: Variance and standard deviation of the different geometries and 217 mAs

<table>
<thead>
<tr>
<th>mode</th>
<th>variance ( \sigma^2 ) [HU]</th>
<th>standard deviation ( \sigma ) [HU]</th>
</tr>
</thead>
<tbody>
<tr>
<td>M08</td>
<td>614.21</td>
<td>24.78</td>
</tr>
<tr>
<td>M03</td>
<td>1.90 \times 10^5</td>
<td>435.62</td>
</tr>
<tr>
<td>M01</td>
<td>1.98 \times 10^5</td>
<td>445.39</td>
</tr>
<tr>
<td>M01s</td>
<td>3.12 \times 10^6</td>
<td>1.77 \times 10^3</td>
</tr>
</tbody>
</table>
6.3. Results

Figure 6.4.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M08 mode and 217 mAs.

Figure 6.5.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M03 mode and 217 mAs.

M08 mode has a maximum resolution of 750 µm although the noise level is very small with $\sigma = 25$ HU. In M03 mode the 250 µm calcification is slightly visible, in the pixel line evaluation it is minimal over noise level which is a lot higher than in macro mode. In contrast, the 250 µm calcification is in M01 mode clearly visible. The difference in noise level $\sigma$ between M03 and M01 mode is thereby just about 10 HU. M01s mode shows strongly increased noise, so than the maximum resolution is about 500 µm. In none of the modes, the soft tissue contrast is high enough to image the glands or their calcifications.
Figure 6.6.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M01 mode and 217 mAs.

Figure 6.7.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M01s mode and 217 mAs.

435 mAs

Here the dose is doubled to 435 mAs, $\sigma^2$ is halved compared to before and the noise $\sigma$ a third lower. The adjusted window width is $W = 4500$ HU with the center at $C = 1500$ HU. Figure 6.8 - Figure 6.11 displays the images for the modes M08, M03, M01 and M01s, as well as Table 6.3 lists the noise ($\sigma^2$, $\sigma$) in the same order.
Table 6.3.: Variance and standard deviation of the different geometries and 435 mAs

<table>
<thead>
<tr>
<th>Mode</th>
<th>Variance $\sigma^2$ [HU]</th>
<th>Standard Deviation $\sigma$ [HU]</th>
</tr>
</thead>
<tbody>
<tr>
<td>M08</td>
<td>353.69</td>
<td>18.81</td>
</tr>
<tr>
<td>M03</td>
<td>$9.41 \cdot 10^4$</td>
<td>306.83</td>
</tr>
<tr>
<td>M01</td>
<td>$9.06 \cdot 10^4$</td>
<td>301.04</td>
</tr>
<tr>
<td>M01s</td>
<td>$2.35 \cdot 10^6$</td>
<td>$1.53 \cdot 10^3$</td>
</tr>
</tbody>
</table>

Figure 6.8.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M08 mode and 435 mAs.

Figure 6.9.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M03 mode and 435 mAs.

M08 mode has still a maximum resolution of 750 µm although the noise level further decreased to $\sigma = 19$ HU. In M03 mode as well as M01 mode the 250 µm calcification is clearly visible, also the 200 µm calcification in the 6 mm gland is identifiable as well as the soft tissue of the glands itself. In M01s mode the noise level of 1530 HU is still too high, so than the maximum resolution stays at 500 µm with no visible glands.
6. Mammography Simulation

Figure 6.10.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M01 mode and 435 mAs.

Figure 6.11.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M01s mode and 435 mAs.

870 mAs

The dose level is now quadrupled to 870 mAs and the noise \( \sigma \) is halved compared to 145 mAs. The adjusted window width is \( W = 4000 \text{ HU} \) with the center at \( C = 1200 \text{ HU} \). Figure 6.12 - Figure 6.15 displays the images for the modes M08, M03, M01 and M01s, as well as Table 6.4 lists the noise \( (\sigma^2, \sigma) \) in the same order.
Table 6.4.: Variance and standard deviation of the different geometries and 870 mAs

<table>
<thead>
<tr>
<th>mode</th>
<th>variance $\sigma^2$ [HU]</th>
<th>standard deviation $\sigma$ [HU]</th>
</tr>
</thead>
<tbody>
<tr>
<td>M08</td>
<td>163.31</td>
<td>12.78</td>
</tr>
<tr>
<td>M03</td>
<td>4.48·10^4</td>
<td>211.70</td>
</tr>
<tr>
<td>M01</td>
<td>4.39·10^4</td>
<td>209.50</td>
</tr>
<tr>
<td>M01s</td>
<td>1.00·10^6</td>
<td>1.00·10^3</td>
</tr>
</tbody>
</table>

Figure 6.12.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M08 mode and 870 mAs.

Figure 6.13.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M03 mode and 870 mAs.

M08 mode increased its resolution of 500 µm, which are still hard to distinguish, although the noise level is halved to $\sigma = 12$ HU compared to 145 mAs. The glands are identifiable. In M03 mode as well as M01 mode the 250 µm and the 200 µm calcification in the 6 mm gland are clearly visible, also the soft tissue contrast for the glands increased. The noise level $\sigma$ of the two modes are nearly the same. In M01s mode the 250 µm cal-
6. Mammography Simulation

Figure 6.14.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M01 mode and 870 mAs.

Figure 6.15.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M01s mode and 870 mAs.

calcification becomes visible despite the high noise of 1000 HU. The noise is still too high for an identification of glands.
6.3. Results

Irrationally High Dose Value

The dose is adjusted to an exceedingly high value of 30000 mAs which is 140 times the usual dose, in order to reduce the noise strongly and to investigate to see the maximum possible resolution of each system with a minimum noise. The adjusted window width is \( W = 2000 \text{ HU} \) with the center at \( C = 600 \text{ HU} \). Figure 6.16 - Figure 6.19 displays the images for the modes M08, M03, M01 and M01s, as well as Table 6.5 lists the noise \((\sigma^2, \sigma)\) in the same order.

<table>
<thead>
<tr>
<th>mode</th>
<th>variance ( \sigma^2 ) [HU]</th>
<th>standard deviation ( \sigma ) [HU]</th>
</tr>
</thead>
<tbody>
<tr>
<td>M08</td>
<td>45.57</td>
<td>6.75</td>
</tr>
<tr>
<td>M03</td>
<td>(1.45 \cdot 10^4)</td>
<td>38.07</td>
</tr>
<tr>
<td>M01</td>
<td>(1.52 \cdot 10^4)</td>
<td>39.03</td>
</tr>
<tr>
<td>M01s</td>
<td>(3.62 \cdot 10^4)</td>
<td>190.35</td>
</tr>
</tbody>
</table>

Figure 6.16.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M08 mode and 30000 mAs.
6. Mammography Simulation

Figure 6.17.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M03 mode and 30000 mAs.

Figure 6.18.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M01 mode and 30000 mAs.

The maximum possible resolution of M08 mode is 500 µm. The noise level is quartered to $\sigma = 6$ HU compared to 145 mAs. The glands are identifiable. M03 mode, as well as M01 mode, show a resolution of 100 µm which is visible in the calcification line and also in the glands, whereby M01 mode exposes higher contrast of the calcifications in the glands. Also the line plots in Figure 6.17(a) and Figure 6.18(a) provide a clear distinction of the 100 µm calcification with a four times higher contrast compared to the noise level. The glands are clearly identifiable. With this irrationally high dose, the noise level $\sigma$ of the M03 and M01 mode is nearly identical. In M01s mode the noise is reduced to the level of 190 HU and provides the highest resolution of all images. The 100 µm calcifications are clearly visible, in the breast tissue and the glands, and the contrast is about eight times higher in comparison to the noise. The glands are clearly identifiable.
6.3. Results

Figure 6.19.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M01s mode and 30000 mAs.

6.3.2. Images with same MTF

For a more direct comparison of the different geometries, the images were reconstructed with W80f kernels providing the same MTF, and therefore the same sharpness, for the geometries M03, M01 and M01s, see Figure 6.20. It is not possible to achieve this sharpness in M08 mode, therefore it is left out. Again, the noises of the images are compared as before. With all images having the same image sharpness, the difference should be recognizable in the noise; the better the scanner geometry the lower the noise. Consequently, M01s mode should have lower noise than M01 mode and M01 also lower noise than M03 mode. The kernel should also provide similar noise levels to M03 and M01 with S80f because the MTF of the W80f is similar to them, for the M01s mode a reduced noise is expected.

217 mAs

The images with the lowest used mAs setting, 217 mAs, are compared. The adjusted window width is W = 3500 HU with the center at C = 1300 HU. Figure 6.21 - Figure 6.23 displays the images for the modes M03, M01 and M01s, as well as Table 6.6 lists the noise ($\sigma^2$, $\sigma$) in the same order.

Table 6.6.: Variance and standard deviation of the different geometries, the same image MTF and 217 mAs

<table>
<thead>
<tr>
<th>mode</th>
<th>variance $\sigma^2$ [HU]</th>
<th>standard deviation $\sigma$ [HU]</th>
</tr>
</thead>
<tbody>
<tr>
<td>M03</td>
<td>2.43·10^5</td>
<td>492.50</td>
</tr>
<tr>
<td>M01</td>
<td>1.34·10^5</td>
<td>365.84</td>
</tr>
<tr>
<td>M01s</td>
<td>2.22·10^5</td>
<td>470.66</td>
</tr>
</tbody>
</table>
6. Mammography Simulation

Figure 6.20.: Image MTF of the W80f kernel for the geometries M03, M01 and M01s.

Figure 6.21.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M03 mode and 217 mAs.

For 217 mAs, M01 mode provides the lowest noise. M01s mode is, albeit slightly below M03 mode, still higher than M01 mode, although the calcification contrast is higher than in HR (see Figure 6.23). The 250 µm calcification is clearly visible in M01 and M01s mode, in M03 mode the noise superimposes the object.

435 mAs

The adjusted window width for 435 mAs is $W = 4500$ HU with the center at $C = 1500$ HU. Figure 6.24 - Figure 6.26 displays the images for the modes M03, M01 and M01s, as well as Table 6.7 lists the noise $(\sigma^2, \sigma)$ in the same order.
6.3. Results

Figure 6.22.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M01 mode and 217 mAs.

Figure 6.23.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M01s mode and 217 mAs.

For 435 mAs the predicted noise behavior, that the system with the highest resolution possibility has the lowest noise, is accurate. The noise level decreases from M03, to M01 and to M01s. In all geometries the 250 µm calcifications are clearly detectable, the 200 µm calcification in the 6 mm gland is also slightly visible.
Table 6.7.: Variance and standard deviation of the different geometries, the same image MTF and 435 mAs

<table>
<thead>
<tr>
<th>mode</th>
<th>variance $\sigma^2$ [HU]</th>
<th>standard deviation $\sigma$ [HU]</th>
</tr>
</thead>
<tbody>
<tr>
<td>M03</td>
<td>$1.22 \cdot 10^5$</td>
<td>349.61</td>
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<tr>
<td>M01</td>
<td>$5.97 \cdot 10^4$</td>
<td>244.30</td>
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<tr>
<td>M01s</td>
<td>$5.19 \cdot 10^4$</td>
<td>227.91</td>
</tr>
</tbody>
</table>

Figure 6.24.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M03 mode and 435 mAs.

Figure 6.25.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M01 mode and 435 mAs.

870 mAs

For a dose of 870 mAs, the adjusted window width is $W = 4000$ HU with the center at $C = 1200$ HU. Figure 6.27 - Figure 6.29 displays the images for the modes M03, M01 and M01s, as well as Table 6.8 lists the noise ($\sigma^2$, $\sigma$) in the same order.
6.3. Results

Figure 6.26.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M01s mode and 435 mAs.

Table 6.8.: Variance and standard deviation of the different geometries, the same image MTF and 870 mAs

<table>
<thead>
<tr>
<th>mode</th>
<th>variance $\sigma^2$ [HU]</th>
<th>standard deviation $\sigma$ [HU]</th>
</tr>
</thead>
<tbody>
<tr>
<td>M03</td>
<td>$5.89 \cdot 10^4$</td>
<td>242.59</td>
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<tr>
<td>M01</td>
<td>$2.90 \cdot 10^4$</td>
<td>170.27</td>
</tr>
<tr>
<td>M01s</td>
<td>$2.22 \cdot 10^4$</td>
<td>148.98</td>
</tr>
</tbody>
</table>

Figure 6.27.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M03 mode and 870 mAs.

For 870 keV, the noise level is also decreasing with increasing system resolution. The 200 µm calcification is now clearly visible in all three geometries, 100 µm can still not be resolved due to the high noise. The soft tissue contrast is also increased.
6. Mammography Simulation

Irrationally High Dose Value

The adjusted window width here is $W = 2000$ HU with the center at $C = 600$ HU. Figure 6.30 - Figure 6.32 displays the images for the modes M03, M01 and M01s, as well as Table 6.9 lists the noise ($\sigma^2, \sigma$) in the same order.

At high dose the noise levels also decline with increasing system geometry and the noise level has declined to a very low level. The the 100 $\mu$m calcification is clearly detectable in all three geometries and, as shown in the line plots, provides a sufficient contrast for a reliable detection. However, the highest resolution is given by the M01s mode.
Table 6.9.: Variance and standard deviation of the different geometries, the same image MTF and 30000 mAs

<table>
<thead>
<tr>
<th>mode</th>
<th>variance $\sigma^2$ [HU]</th>
<th>standard deviation $\sigma$ [HU]</th>
</tr>
</thead>
<tbody>
<tr>
<td>M03</td>
<td>1.85 $\cdot 10^4$</td>
<td>43.03</td>
</tr>
<tr>
<td>M01</td>
<td>1.06 $\cdot 10^3$</td>
<td>32.54</td>
</tr>
<tr>
<td>M01s</td>
<td>687.68</td>
<td>26.22</td>
</tr>
</tbody>
</table>

Figure 6.30.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M03 mode and 30000 mAs.

Figure 6.31.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M01 mode and 30000 mAs.
Figure 6.32.: (a) Pixel line of microcalcifications. (b) Reconstructed phantom in M01s mode and 30000 mAs.
6.3. Discussion of Results

With the simulation software and the detector model different new geometries were investigated to find a setting providing a desired detectability of 100 µm. For this purpose a complete thorax was simulated, including the breast with calcification spheres in the order of 100 µm. The images were reconstructed with a sharp kernel reaching up to the highest possible resolution and a second kernel with constant image MTF for direct comparison of the different systems. The currents varied from actual thorax scan values to a multiples of it.

**Feasibility** The new, smaller geometries M03, M01 and M01s provide a distinct higher resolution, compared to M08 mode. Especially images with highly reduced noise at very high dose levels demonstrate the resolution of 100 µm. This and the lack of artifacts confirms that the simulation and the detector model image the geometries correctly. Even in M03 mode with 300 µm focus diameter and 225 µm pixel size the 100 µm calcifications are visible. With the S80f kernel, it can be observed that the difference in noise, which limits the resolution, is very small between sharp and M01 mode for all dose levels. In a further evaluation the sharpness is set constant for all images by reconstructing them with a W80f kernel with the same MTF. It was expected, that image noise is now the only difference between the images and that smaller geometries subsequently have lower noise. Except for the 217 mAs image of M01s mode, this is consistent throughout all geometries and dose levels. In this single case, the noise increase is caused by photon starvation occurring earlier at small pixel sizes. This is a well known, intrinsic property of CT reconstruction. The noise level of M01 and M03 is comparable to the S80f reconstruction, M01s provides a strongly reduced noise compared to the S80f kernel. For images with high noise and low dose (217 mAs), only M01 mode provides a resolution of 250 µm. It needs a doubled dose of 435 mAs to identify the 250 µm calcification in M03 mode.

**Clinical Relevance** Exposing patients to a minimum amount of dose as possible is the highest priority of x-ray imaging. The goal was providing a detectability of 100 µm calcifications while not using more dose than in a clinical thorax scan typically needed. Only the 217 mAs case comes close to this. Here, the M01 mode provides the highest detectability down to 250 µm. M08, M03 and M01s mode are not able to resolve this. For an even higher detectability, at least the doubled dose is required. There, M03 and M01 mode are able to detect objects down to 200 µm.

It has to be noted that these results only represent an idealized system in a simulation framework. Although the applied dose values were adjusted to comparable measurements, the conditions were idealized by neglecting patient movement, assuming stable x-ray foci, especially in M01s.
In this thesis, a simulation study regarding the resolution capability of whole-body CTs equipped with PCDs was performed. Thereby it was investigated, whether the resolution of these systems is high enough to get clinically useful information of the breast at clinically accepted dose levels. One determining factor for this is a resolution of around hundred micrometer as needed for mammography examination. The images might be acquired by a specific breast imaging mode adjusted at the scanner or result from a routine scan of the thorax where the breasts typically are within the range of the scan. An intrinsic advantage of whole-body CT imaging is its ability to cover the region towards shoulder which is not fully included within dedicated breast screening devices. Therefore, new detector and tube geometries were tested using a new detector model for PCDs.

In the first part of this thesis, this newly developed detector model for PCD was validated. It takes into account the spatio-energetic cross talk between pixels. For the validation, measurements were made at a real scanner prototype as a reference. Settings of the measurements and simulations were the same for comparison. The simulation thereby revealed a variance of the CT values which was lower by a third compared to the measurements. With the variance being indirect proportional to the dose, this leads to a calibration factor of 1.5 in simulated dose values. Additionally, a systematic shift of about 5 keV was discovered for the adjustment of the upper energy threshold. The difference was evaluated by noise comparisons, threshold correlations and CT values. Taking in account the 1.5 dose factor and the difference in the upper threshold settings, the simulation was adjusted and ready to be used for further studies.

In the second part the detector model was used to investigate the resolution capability of whole-body CTs with PCDs for different x-ray tube and detector geometries. Therefore, focus and pixel size as well as the slice width are varied, as they are relevant to the spatial resolution. A synthetic thorax phantom was created, including glands and calcification spheres with realistic contrast values in the order of 100 µm in the breast. The phantom was simulated with dose values starting at 217 mAs to a distinctly exceeding dose to compare the resolution for relevant dose levels as well as the maximum possible at a high noise reduction. The geometries are varied from typical, already configurations adjustments in CT systems with a 0.8 mm focus diameter and 900 µm pixel size, down to a hypothetical 0.1 mm focus diameter and 100 µm pixel size. The images were reconstructed with a kernel exploiting maximum sharpness for each geometry and another kernel with the same image MTF. The results of the new geometry systems show significant improvement in resolution compared to the conventional systems. Objects down to the order of 250 µm can be resolved by reducing the focus to 0.3 mm or smaller.
and the pixel size to 225 µm at a dose of 217 mAs and a voltage of 120 kV. In contrast, conventional geometries resolve about 750 µm at the same conditions. As expected, in the smallest geometry with 100 µm pixel size and 0.1 mm focus diameter the noise in sharp CT images is highly increased and superimposes most of the calcifications at low dose levels. The desired 100 µm can be resolved by all new geometries using irrationally high dose levels, but at clinically relevant dose levels none of the geometries was able to resolve such small structures at realistic contrast values.

Overall, the study showed promising results for the resolution capability of whole body CTs with implemented PCDs - down to 250 µm are resolvable at reasonable dose levels. Increasing the dose to increase resolution is thereby not reconcilable with exposing the patient to additional ionizing radiation. As the 300 µm focus adjustment provides a similar resolution as with 100 µm, enabling a focus size of 300 µm may be sufficient for further considerations. The 225 µm pixel size is already applicable in the detector as they represent the subpixels in the existing geometry.

The desired hundred micrometer for mammography purposes cannot be detected in any of the investigated scenarios with reasonable dose levels. The increased noise level caused by the x-ray beam attenuated by the whole thorax and not only the breast, acts as the limiting factor. For now, other, dedicated screening modalities provide a higher resolution at less dose compared to a whole-body CT scan. A special breast imaging mode in whole-body CT providing reliable, clinically useful information is therefore not achievable. But if thorax scans with the breast in the range of the scan are performed anyway, the resolution can be sufficient that the images could provide information on the presence of malignancies. Although the desired detectability of 100 µm were unlikely to achieve, the effort to investigate whole-body CT as a breast imaging modality was not spared; the region between the breast towards the shoulder is still not completely examinable in dedicated breast imaging methods.
# A. Appendix

## A.1. TNM Classification of Carcinomas of the Breast

<table>
<thead>
<tr>
<th>TNM Classification of Carcinomas of the Breast</th>
<th>M  – Distant Metastasis</th>
<th>MX – Distant metastasis cannot be assessed</th>
<th>M0 – No distant metastasis</th>
<th>M1 – Distant metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1 Tumour 2 cm or less in greatest dimension</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1a Microinvasion 0.1 cm or less in greatest dimension</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1b More than 0.1 cm but not more than 0.5 cm in greatest dimension</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T1c More than 1 cm but not more than 2 cm in greatest dimension</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2 Tumour more than 2 cm but not more than 5 cm in greatest dimension</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T3 Tumour more than 5 cm in greatest dimension</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T4 Tumour of any size with direct extension to chest wall or skin only as described in T4a to T4d</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: TNM classification is based on the size and location of the tumour, as well as the presence or absence of metastases. The classification is based on the following:

- **M** – Distant Metastasis
- **MX** – Distant metastasis cannot be assessed
- **M0** – No distant metastasis
- **M1** – Distant metastasis

### TNM Clinical Classification

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Tumour 2 cm or less in greatest dimension</td>
</tr>
<tr>
<td>T1a</td>
<td>Microinvasion 0.1 cm or less in greatest dimension</td>
</tr>
<tr>
<td>T1b</td>
<td>More than 0.1 cm but not more than 0.5 cm in greatest dimension</td>
</tr>
<tr>
<td>T1c</td>
<td>More than 1 cm but not more than 2 cm in greatest dimension</td>
</tr>
<tr>
<td>T2</td>
<td>Tumour more than 2 cm but not more than 5 cm in greatest dimension</td>
</tr>
<tr>
<td>T3</td>
<td>Tumour more than 5 cm in greatest dimension</td>
</tr>
<tr>
<td>T4</td>
<td>Tumour of any size with direct extension to chest wall or skin</td>
</tr>
</tbody>
</table>

### TNM Pathological Classification

<table>
<thead>
<tr>
<th>pT  – Primary Tumour</th>
<th>pN – Regional Lymph Nodes</th>
<th>pM – Distant Metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>pT1</td>
<td>pN0</td>
<td>pM0</td>
</tr>
<tr>
<td>pT2</td>
<td>pN1</td>
<td>pM1</td>
</tr>
<tr>
<td>pT3</td>
<td>pN2</td>
<td>pM2</td>
</tr>
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<td>pM3C</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Note: Pathological classification is based on the size and location of the tumour, as well as the presence or absence of metastases. The classification is based on the following:

- **pT** – Primary Tumour
- **pN** – Regional Lymph Nodes
- **pM** – Distant Metastasis

### TNM Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>pT1</td>
<td>Tumour 2 cm or less in greatest dimension</td>
</tr>
<tr>
<td>pT2</td>
<td>Tumour more than 2 cm but not more than 5 cm in greatest dimension</td>
</tr>
<tr>
<td>pT3</td>
<td>Tumour more than 5 cm in greatest dimension</td>
</tr>
<tr>
<td>pT4</td>
<td>Tumour of any size with direct extension to chest wall or skin</td>
</tr>
</tbody>
</table>

Note: TNM staging is based on the size and location of the tumour, as well as the presence or absence of metastases. The staging is based on the following:

- **pT** – Primary Tumour
- **pN** – Regional Lymph Nodes
- **pM** – Distant Metastasis

### TNM Classification

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
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<tbody>
<tr>
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</tr>
<tr>
<td>T1a</td>
<td>Microinvasion 0.1 cm or less in greatest dimension</td>
</tr>
<tr>
<td>T1b</td>
<td>More than 0.1 cm but not more than 0.5 cm in greatest dimension</td>
</tr>
<tr>
<td>T1c</td>
<td>More than 1 cm but not more than 2 cm in greatest dimension</td>
</tr>
<tr>
<td>T2</td>
<td>Tumour more than 2 cm but not more than 5 cm in greatest dimension</td>
</tr>
<tr>
<td>T3</td>
<td>Tumour more than 5 cm in greatest dimension</td>
</tr>
<tr>
<td>T4</td>
<td>Tumour of any size with direct extension to chest wall or skin</td>
</tr>
</tbody>
</table>

Note: TNM classification is based on the size and location of the tumour, as well as the presence or absence of metastases. The classification is based on the following:

- **T** – Primary Tumour
- **N** – Regional Lymph Nodes
- **M** – Distant Metastasis

### TNM Staging

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>Tumour 2 cm or less in greatest dimension</td>
</tr>
<tr>
<td>T1a</td>
<td>Microinvasion 0.1 cm or less in greatest dimension</td>
</tr>
<tr>
<td>T1b</td>
<td>More than 0.1 cm but not more than 0.5 cm in greatest dimension</td>
</tr>
<tr>
<td>T1c</td>
<td>More than 1 cm but not more than 2 cm in greatest dimension</td>
</tr>
<tr>
<td>T2</td>
<td>Tumour more than 2 cm but not more than 5 cm in greatest dimension</td>
</tr>
<tr>
<td>T3</td>
<td>Tumour more than 5 cm in greatest dimension</td>
</tr>
<tr>
<td>T4</td>
<td>Tumour of any size with direct extension to chest wall or skin</td>
</tr>
</tbody>
</table>

Note: TNM staging is based on the size and location of the tumour, as well as the presence or absence of metastases. The staging is based on the following:

- **T** – Primary Tumour
- **N** – Regional Lymph Nodes
- **M** – Distant Metastasis
<table>
<thead>
<tr>
<th>Stage Grouping</th>
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<th>N0</th>
<th>M0</th>
</tr>
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<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIA</td>
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<td>M0</td>
</tr>
<tr>
<td>Stage IIB</td>
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<td>M0</td>
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<tr>
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<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIB</td>
<td>T0</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IIIC</td>
<td>T1</td>
<td>N2</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IV</td>
<td>Any T</td>
<td>N3</td>
<td>M0</td>
</tr>
</tbody>
</table>

The regional lymph nodes are:

1. Auxiliary (ipsilateral) interpectoral (Rotter) nodes and lymph nodes along the axillary vein and its tributaries, which may be divided into the following levels:
   - Level I (low-anterior) lymph nodes lateral to the lateral border of pectoralis minor muscle.
   - Level II (mid-anterior) lymph nodes between the medial and lateral borders of the pectoralis minor and muscle and the interpectoral (Rotter) lymph nodes.
   - Level III (superior axillary) spinal lymph nodes and those medial to the medial margin of the pectoralis minor muscle, excluding those designated as subclavicular or infraclavicular.

Note: Intramammary lymph nodes are coded as auxiliary lymph nodes, level I.

2. Infraclavicular (subclavicular) (ipsilateral).
3. Internal mammary (ipsilateral) lymph nodes in the intercostal spaces along the edge of the sternum in the endothoracic fascia.
4. Supracleavicular (ipsilateral).

*The pathological N classification requires the resection and examination of at least the low axillary lymph nodes (level I). Examination of one or more sentinel lymph nodes may be used for pathological classification. If classification is based solely on sentinel node biopsy without subsequent axillary lymph node dissection it should be designated (n) for sentinel node, e.g. pT(n)N(n).*

*1/1/2016.*

*A help desk for specific questions about the TNM classification is available at [http://tnm.uicr.org.](http://tnm.uicr.org).*
A.2. Absolute Noise Variances

Figure A.1.: (a) Absolute noise values $\sigma^2$ in lower and higher threshold of measurement and simulation. (b) Simulation noise $\sigma^2$ scaled by factor 1.5.

Figure A.2.: Absolute noise values in lower and higher threshold of measurement and simulation, simulation scaled by factor 1.5 and additionally shifted by (a) 3 keV and (b) 5 keV.
Figure A.3.: (a) Absolute noise values $\sigma^2$ in lower and higher threshold of measurement and simulation. (b) Simulation noise $\sigma^2$ scaled by factor 1.5.

Figure A.4.: Absolute noise values in lower and higher threshold of measurement and simulation, simulation scaled by factor 1.5 and additionally shifted by (a) 3 keV and (b) 5 keV.
A.3. Normalized Noise Variances

Figure A.5.: Relative noises $\sigma^2$ of water of the simulation and measurement are compared for each energy threshold combination.

Figure A.6.: Relative noises $\sigma^2$ in water. Upper energy thresholds of the simulation are lowered by (a) 3 keV and (b) 5 keV.
Figure A.7.: Relative noises $\sigma^2$ of water of the simulation and measurement are compared for each energy threshold combination.

Figure A.8.: Relative noises $\sigma^2$ in water. Upper energy thresholds of the simulation are lowered by (a) 3 keV and (b) 5 keV.
A.4. Normalized Covariances

Figure A.9.: Normalized covariances for each threshold combination of measurement data (red), simulation data (blue) and shifted simulation data (green) by (a) 3 keV and (b) 5 keV.

Figure A.10.: Normalized covariances for each threshold combination of measurement data (red), simulation data (blue) and shifted simulation data (green) by (a) 3 keV and (b) 5 keV.
A.5. CT Values of Iodine

Figure A.11.: CT values of iodine as measured, simulated and simulated with 3 and 5 keV differences respectively. Higher and lower thresholds plotted against each other for each set of threshold combination with lower threshold (a) 35 keV and lower threshold (b) 45 keV
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Bibliography


[7] Allan MacLeod Cormack. “Representation of a function by its line integrals, with some radiological applications”. In: Journal of applied physics 34.9 (1963), pp. 2722–2727.


