Evaluation of Photon-Counting Spectral Breast Tomosynthesis

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Abstract

The superposition of anatomical structures often greatly impedes detectability in conventional mammography. Spectral imaging and tomosynthesis are two promising methods used for suppression of the anatomical background. The aim of this thesis is to compare and evaluate the benefits of tomosynthesis and spectral imaging, both in combination and separately. A computer model for signal and noise transfer in tomosynthesis was developed and combined with an existing model for spectral imaging. Measurements were performed to validate the models. An ideal-observer detectability index incorporating anatomical noise was used as a figure of merit to compare the different modalities. For detection of a contrast-enhanced tumor in a breast with high anatomical background, the optimum performance for spectral tomosynthesis was found at a tomo-angle of 10 degrees. The improvement was in the order of a factor 10 compared to non-energy-resolved tomosynthesis with the same angular extent. This was supported by clinical results.

Contents

Contents	iv
1 Introduction	1
1.1 Mammography	1
1.2 Digital Mammography	1
1.3 Spectral Imaging	2
1.4 Tomosynthesis	2
1.5 Outline of the Thesis	3
2 Imaging Performance Assessment	5
2.1 Modulation Transfer Function	5
2.2 Noise-Power Spectrum	6
2.3 Detectability	6
3 Spectral Imaging	9
3.1 Introduction	9
3.2 Materials and Methods	9
3.2.1 Description of the System	9
3.2.2 System Modeling	10
Spectral imaging	10
Alternative derivation of w_{1/S_A}^*	11
3.2.3 The Tissue Phantom	12
3.2.4 Imaging Performance Metrics	13
3.3 Results and Discussion	14
3.4 Conclusions	17
4 Spectral Tomosynthesis	19
4.1 Introduction	19

4.2	Materials and Methods	19
4.2.1	Description of the System	19
4.2.2	System Modeling	20
	Signal and Noise Transfer in Tomosynthesis	20
	Ideal-Observer Detectability	22
4.2.3	Measurements	22
	NPS and MTF	23
	Spectral Tomosynthesis: Clinical Images	23
4.3	Results and Discussion	23
4.3.1	Measurements	23
	NPS and MTF	23
	Spectral Tomosynthesis: Clinical Images	23
4.3.2	System Modeling	24
4.4	Conclusions	25
	Bibliography	29

Chapter 1

Introduction

1.1 Mammography

Breast cancer accounted for 29% of the cancer incidence among Swedish women 2009 [1], and it is the the second most common cause of cancer death [2]. An effective way of reducing breast cancer mortality is mammography screening, since early detection improves the chances of successful treatment. In populations that have undergone yearly interval screening mammography, the mortality reduction is 25-30% [3]. Still 20-40% of the breast cancers are initially missed, and there is also a large amount of healthy patients that are recalled for additional examinations.

Different modalities can be used for breast imaging, but when it comes to screening, x-ray imaging seems more feasible than magnetic resonance imaging and ultrasonography. The former is expensive and often require injection of a contrast agent, and the latter is highly operator-dependent and time-consuming. Additionally, x-ray mammography provides images with high spatial resolution [4].

Mammography is, however, one of the most technically demanding x-ray imaging techniques [5]. One of the challenges is to acquire good contrast, since the difference in x-ray attenuation of the target is small. Additionally, the imaging system has to be capable of visualizing small microcalcifications and thin tumor fibers, which puts high demands on spatial resolution. Furthermore, in screening, when examining a large population, it is of great importance to minimize the radiation dose.

1.2 Digital Mammography

Even though digital mammography is not a new idea, it was not until 2006 that it was approved by the Food and Drug Administration in the USA. One of the problems was to get equal spatial resolution as in conventional screen-film mammography. Today the digital systems are taking over, and there are different detector technologies in use. In energy-integrating detectors, the charge that is released when photons hit the detector is summed over the exposure time. This also means that any electronic noise is integrated with the signal. Photon-counting detectors on the other hand are fast enough to detect one photon at a time, and by implementing an energy threshold, the electronic noise can be eliminated.

1.3 Spectral Imaging

Another advantage of photon-counting detectors is the possibility of performing energy weighting. By implementing a second threshold, low- and high-energy photons can be distinguished from one another. This makes it possible to assign greater weight to the low-energy photons, which carry more contrast information [4]. On the contrary, energy integrating detectors will actually give the high-energy photons larger weight since the charge released by photons is proportional to its energy.

Energy weighting aims at optimizing the contrast relative to the noise caused by the random fluctuation of x-ray emission, referred to as quantum noise. However, in 2-dimensional (2D) imaging, the superposition of anatomical structures is often more problematic than quantum noise [6, 7]. In a 2D mammogram for example, a tumor may be difficult to detect because normal tissue structures may obscure or hide it, and may also superimpose and appear as a pathology. Dual-energy subtraction (DES) [8, 9] is a method for reducing this anatomical background. In DES mammography, the anatomical background is suppressed by minimizing the contrast between adipose and glandular tissue. This is done by combining two images acquired with different x-ray spectra into a weighted subtraction image, with an appropriate choice of weight factor. The framework is similar to energy weighting, but in this scheme, the weight factor has opposite sign.

With a photon-counting detector, which sorts the photons into a high- and a low-energy bin, one can simultaneously acquire a high- and a low-energy image which can be used for spectral imaging. Often the weight is chosen to optimize the signal-to-noise-ratio (SNR), taking both quantum and anatomical noise into account. It is of course also possible to form an unweighted sum of the images, in which case a conventional non-energy resolved image is acquired.

1.4 Tomosynthesis

Tomosynthesis [10–16] is another method used for reduction of anatomical background. By acquiring several 2D images from different angles, a 3-dimensional (3D) image can be reconstructed. This makes it possible for the physician to analyze one slice of the patient at a time, hence suppressing anatomical structures from above and below this slice.

Tomosynthesis is similar to cone-beam computed tomography (CBCT), but is limited in angular range and uses fewer projections. While CBCT suppresses all out-of-plane structures, tomosynthesis only partially accomplishes this. On the other hand, a tomosynthesis examination has the benefit of lower patient dose compared to a CBCT examination.

The idea of tomography is quite old. In 1917, Radon introduced the mathematical framework for tomography, and in the 1930s tomographic imaging was recognized as a valuable imaging modality. In early tomography, the x-ray source, continuously emitting radiation, and film were moved around the patient in such a way that all anatomical structures except those from a selected plane of the patient were projected on different positions of the film, making them blurred [10]. The anatomy in the focal plane, on the other hand, appeared stationary and was more sharply imaged. However, one of the drawbacks of this technique is that only one slice can be imaged at a time, leading to high doses if images of more planes are needed. Secondly, out-of-plane structures are not satisfactory suppressed.

The theory of how to reconstruct an arbitrary number of planes from a set of discrete

2D projections had been around for long until tomosynthesis was finally realized in practice in the late 1960s. Today the interest in tomosynthesis is increasing, and its application in mammography is promising.

1.5 Outline of the Thesis

The aim of this thesis is to evaluate a mammography system combining tomosynthesis with spectral imaging. In the next chapter, theory for imaging performance assessment is reviewed. Spectral imaging is discussed in Chapter 3, where a tissue phantom study is presented. The measurements are compared with predictions of a model for spectral imaging. In the last chapter, a computer model for tomosynthesis is developed and combined with the spectral imaging model in an effort to investigate the potential of spectral tomosynthesis.

Chapter 2

Imaging Performance Assessment

2.1 Modulation Transfer Function

The point-spread function (PSF) of an imaging system is the intensity distribution in the image when a point object is being imaged. Since the PSF describes the output of the system when the input is an impulse, it is sometimes also referred to as the impulse response function [17].

The intensity distribution, radiating out from an object being imaged with an x-ray system, can mathematically be represented as a sum of points with different intensities. Assuming linearity and a shift-invariant PSF, the output of the imaging system is

$$I_{out}(\mathbf{x}) = \sum_n I_{in}(\mathbf{x}_n) \times \text{PSF}(\mathbf{x} - \mathbf{x}_n), \quad (2.1)$$

which in integral form is written as

$$I_{out}(\mathbf{x}) = \int I_{in}(\mathbf{x}') \times \text{PSF}(\mathbf{x} - \mathbf{x}') d\mathbf{x}' = I_{in}(\mathbf{x}) * \text{PSF}(\mathbf{x}), \quad (2.2)$$

where $*$ denotes convolution. The convolution theorem states that under certain conditions, the Fourier transform of a convolution equals the product of the Fourier transforms of the two functions in the convolution integral. Using this theorem, and defining the optical transfer function (OTF) as the Fourier transform of the PSF, we see that the Fourier transform of Eq. (2.2) is simply

$$\hat{I}_{out}(\mathbf{f}) = \hat{I}_{in}(\mathbf{f}) \times \text{OTF}(\mathbf{f}), \quad (2.3)$$

where $\hat{I}$ denotes the Fourier transform of I and $\mathbf{f}$ the spatial frequency. Now, define the modulation transfer function (MTF) as the absolute value of the OTF. By taking the modulus of Eq. (2.3) we then finally get

$$|\hat{I}_{out}(\mathbf{f})| = T(\mathbf{f}) \times |\hat{I}_{in}(\mathbf{f})|, \quad (2.4)$$

where T denotes the MTF. From Eq. (2.4) we see that $T(\mathbf{f})$ can be interpreted as the gain factor between the input and the output, for the spatial frequency $\mathbf{f}$. In other words, the MTF describes how much a certain spatial frequency component is modulated in amplitude by the imaging system and is therefore a measure of how well the system reproduces objects

with this spatial frequency. It is standard to normalize the MTF to unity for the zero-frequency. The ideal MTF would therefore be equal to one for all frequencies, but this is never the case in practice. The MTF falls off to zero for high frequencies, and the frequency above which the MTF equals zero is called the limiting frequency. Objects smaller than the size corresponding to this frequency cannot be reproduced by the system. A similar resolution limit could also be acquired through the Rayleigh criterion, but this criterion says nothing about what happens to lower spatial frequencies. In fact, a high MTF also for lower frequencies is important for the image quality.

As it turns out, it is advantageous to work in the spatial frequency domain. The MTF is a very convenient way of characterizing the signal transfer of a system. We now also need a way of quantifying noise as a function of frequency.

2.2 Noise-Power Spectrum

The emission of photons is a stochastic process, which means that the number of photons radiating from an x-ray source is subject to random fluctuations. In an x-ray imaging system, this adds noise to the image. In order to characterize this, the quantum noise-power spectrum (NPS) is introduced. It can be defined as an ensemble average over N acquired images,

$$S_Q(\mathbf{f}) = \lim_{N \rightarrow \infty} \frac{1}{N} \sum_{n=1}^N |\hat{I}_n(\mathbf{f})|^2, \quad (2.5)$$

where $\hat{I}_n(\mathbf{f})$ is the Fourier transform of a mean-subtracted noise-only image. Note that S_Q carries units of signal squared.

Another factor that often impedes the imaging task more than S_Q , is the anatomical background. That is, structures in the image due to other anatomy which is of no interest, and only complicates the imaging task. A common approach to take this into account is to introduce the anatomical NPS as [6, 7, 18]

$$S_A(f_r) = \frac{\alpha}{f_r^\beta}, \quad (2.6)$$

where α and β are parameters, which are empirically determined and f_r is the radial frequency. S_A carries the same units as S_Q .

2.3 Detectability

We now have tools for characterizing the signal and noise in the spatial frequency domain. By introducing the noise-equivalent quanta (NEQ) as

$$\text{NEQ}(\mathbf{f}) = \frac{\langle I \rangle^2 T^2(\mathbf{f})}{S_Q(\mathbf{f})}, \quad (2.7)$$

we have defined the squared signal-to-noise-ratio (SNR) of the system. Here $\langle I \rangle$ denotes the expected image signal.

To incorporate the anatomical background into the performance evaluation, a generalized NEQ (GNEQ) can be defined as [8, 9]

$$\text{GNEQ}(\mathbf{f}) = \frac{\langle I \rangle^2 T^2(\mathbf{f})}{S_Q(\mathbf{f}) + T^2(\mathbf{f}) S_A(\mathbf{f})}, \quad (2.8)$$

where the anatomical noise term is simply added to the quantum noise term. Note that the anatomical noise is a part of the imaged object, and therefore should be multiplied by the squared MTF. The $\text{GNEQ}(\mathbf{f})$ can be interpreted as the SNR, taking anatomical noise into account, for the spatial frequency $\mathbf{f}$. In systems where the electronic noise can not be neglected, an electronic noise term should be added in the denominator of Eq. (2.8).

The ultimate goal of medical imaging is to successfully perform a given imaging task. This task could for example be detection of a tumor. In order to evaluate how well an imaging system achieves this goal, the GNEQ can be used to define an ideal-observer detectability index [8, 9]

$$d'^2 = \int \text{GNEQ}(\mathbf{f}) \times F^2(\mathbf{f}) \times C^2 d\mathbf{f}, \quad (2.9)$$

where $F(\mathbf{f})$ is the task function, essentially the Fourier transform of the target geometry, and $C = \Delta s / \langle I \rangle$, with Δs being the target-to-background signal difference.

Intuitively, d' is the SNR for the considered task, taking all frequencies into account. The detectability index can be used to calculate the area under a receiver operating characteristic (ROC) curve, which describes how well the imaging task is performed in terms of sensitivity and specificity (true or false positive rates). Naturally, a large value of d' corresponds to a large area under the ROC curve and better performance.

Chapter 3

Spectral Imaging

3.1 Introduction

Spectral imaging takes advantage of the difference in the energy dependencies of the x-ray attenuation of different materials. The contrast between any two materials can be reduced by a weighted subtraction of two images acquired with different x-ray spectra. In mammography, the anatomical background consists of adipose and glandular tissue, and by reducing the contrast between these two materials, the anatomical noise is suppressed. The weight factor should be chosen to optimize the target-signal-to-noise-ratio, which will depend on both anatomical and quantum noise [9]. The minimum level of performance of spectral imaging corresponds to using the weight factor that gives the standard non-energy-resolved image.

3.2 Materials and Methods

3.2.1 Description of the System

In this study, a Sectra MicroDose Mammography (MDM) system was used. A photograph and schematic picture of the system is shown in Fig. 3.1. The system incorporates a tungsten anode x-ray tube with a 0.5 mm aluminum filter. The beam is divided into 21 line beams by a pre-collimator. The slits in the pre-collimator are aligned with those in a post-collimator, providing a geometry with intrinsic scatter rejection. The detector consists of silicon-strip detector lines aligned to the collimators. The x-ray tube, collimators and detector are attached to a common arm, and by a scanning motion, a full-field image is acquired.

When a photon impinge on the detector, electron-hole pairs are created. Because of the bias voltage that is applied over the detector material, the charges drift to the anode and the cathode. The preamplifier and shaper are fast enough to collect this charge from one photon at a time and convert the charge to a pulse with a height proportional to the energy of the photon. In the discriminator, pulses below a few keV are rejected as noise. This means that the system has no electronic noise and is thus quantum-limited. Because two neighboring strips may collect charge from the same photon (charge sharing), an anti-coincident logic is implemented to prevent double counting. In the event of charge sharing, the photon is registered only to the strip that collected most charge. This improves the

Figure 3.1: The Sectra MDM system and a schematic of the detector. Photo courtesy of Sectra Mamea AB.

spatial resolution, but worsens the energy resolution. Finally the photons are divided into a low- and a high-energy bin and counted separately. In this way, low- and high-energy images are acquired simultaneously.

3.2.2 System Modeling

A framework to characterize the performance of the system for spectral mammography has been developed by Fredenberg *et al.* The model is summarized below, but the reader is referred to Refs. [9, 19, 20] for a more comprehensive description.

Spectral imaging

Energy weighting and energy subtraction were briefly introduced in Chapter 1. Somewhat simplified, energy weighting ignores S_A and maximizes C^2/S_Q , whereas energy subtraction instead minimizes S_A .

If the low- and high-energy images are normalized with the expected number of counts from mean breast tissue, a combined image with zero mean can be formed according to

$$I(x, y) = w \frac{n_{lo}(x, y)}{\langle n_{lo} \rangle} + \frac{n_{hi}(x, y)}{\langle n_{hi} \rangle} - (w + 1) \simeq w \ln \left[\frac{n_{lo}(x, y)}{\langle n_{lo} \rangle} \right] + \ln \left[\frac{n_{hi}(x, y)}{\langle n_{hi} \rangle} \right], \quad (3.1)$$

where w is a weight factor and n_{lo} and n_{hi} are the low- and high-energy images, respectively. The approximation is valid for small signal differences, $|n_\Omega - \langle n_\Omega \rangle| \ll 1$, where $\Omega \in \{lo, hi\}$ denotes the detector energy bin. Written this way, it is evident that a linear combination, which is the common form for energy weighting, is approximately equal to combination in the logarithmic domain, which is often used for energy subtraction. Energy weighting and energy subtraction can therefore be regarded as special cases of a general image combination.

In the practical case, a combination of the non-normalized images is more handy, i.e.

$$I'(x, y) = w' n_{lo}(x, y) + n_{hi}(x, y) \quad \text{or} \quad I''(x, y) = w'' \ln n_{lo}(x, y) + \ln n_{hi}(x, y). \quad (3.2)$$

The image mean of I , I' , and I'' differ, but the detectability indices calculated with all three image combinations are the same. Note that $I'(w' = 1)$ is a conventional non-energy-resolved absorption image.

If we assume no correlation between the energy bins, the quantum noise in the combined image is

$$S_Q(\mathbf{f}) = \sum_{\Omega} \left. \frac{\partial I}{\partial n_{\Omega}} \right|_{\bar{n}_{\Omega}}^2 \times S_{Q\Omega}(\mathbf{f}) \simeq \left[\frac{w^2}{n_{lo}} + \frac{1}{n_{hi}} \right]. \quad (3.3)$$

The approximation in Eq. (3.3) is for spatially uncorrelated noise.

The anatomical noise in an x-ray image of breast tissue is caused by the variation in glandularity, which is transferred to the image through $I(g(x, y))$, with $g(x, y)$ being the glandular volume fraction as a function of spatial image coordinates x and y . We therefore adopt the power spectrum of $g(x, y)$ as a glandularity NPS ($S_{Ag}(f_r)$), which is transferred to the image NPS ($S_A(f_r)$) according to

$$S_A(f_r) \simeq \left\langle \left. \frac{dI}{dg} \right|^2 \right\rangle \times S_{Ag}(f_r) T^2(f_r) \simeq d_b^2 [w \Delta \bar{\mu}_{ag,lo} + \Delta \bar{\mu}_{ag,hi}]^2 \times S_{Ag}(f_r) T^2(f_r), \quad (3.4)$$

where d_b is the breast thickness, $\Delta \bar{\mu}_{ag,\Omega} \equiv \bar{\mu}_{a,\Omega} - \bar{\mu}_{g,\Omega}$ is the difference in effective linear attenuation between adipose and glandular tissue, and the angle brackets represent the expectation value over the glandularity range. The first approximation of Eq. (3.4) is for piecewise linearity of $I(g)$. The second approximation assumes linearity across the range of glandularities, image combination according to Eq. (3.1), and small signal differences.

Maximization of $\Delta s^2/S_Q$ and $1/S_A$ yields the optima for energy weighting and energy subtraction, respectively:

$$w_{\Delta s^2/S_Q}^* = \zeta_{lo} \Delta \bar{\mu}_{bc,lo} / \zeta_{hi} \Delta \bar{\mu}_{bc,hi}, \quad \text{and} \quad w_{1/S_A}^* = -\Delta \bar{\mu}_{ag,hi} / \Delta \bar{\mu}_{ag,lo}, \quad (3.5)$$

where ζ is the expected fraction of incident counts to be detected. S_A can in practice not be completely eliminated according to Eq. (3.5) because the latter is based on the linear approximation of $I(g)$ in Eq. (3.4).

Alternative derivation of w_{1/S_A}^*

Consider the task of making an image of the simple object shown in Fig. 3.2 [21]. Suppose that we would want there to be no contrast between the tissues with linear attenuation μ_1 and μ_2 . Assume that two images are acquired with two different mono-energetic beams, one with low and one with high energy. Lambert-Beers Law states that the x-ray attenuation for the low-energy beam through path 1 and 2 will be

$$\begin{aligned} n_{lo,1} &= n_{lo,0} e^{-\mu_1(E_{lo})D} \\ n_{lo,2} &= n_{lo,0} e^{-\mu_1(E_{lo})(D-d) - \mu_2(E_{lo})d} \end{aligned}$$

Figure 3.2: Object composed of three different tissue types.

respectively, and analogous for the high-energy beam. For path 1 and 2, I'' becomes

$$\begin{aligned} I_1'' &= w(\ln(n_{lo,0}) - \mu_1(E_{lo})D) + \ln(n_{hi,0}) - \mu_1(E_{hi})D \\ I_2'' &= w(\ln(n_{lo,0}) - \mu_1(E_{lo})(D-d) - \mu_2(E_{lo})d) \\ &\quad + (\ln(n_{hi,0}) - \mu_1(E_{hi})(D-d) - \mu_2(E_{hi})d). \end{aligned}$$

By setting $I_1'' = I_2''$ and solving for w'' , we get

$$w_{1/S_A}^* = -\frac{\mu_1(E_{hi}) - \mu_2(E_{hi})}{\mu_1(E_{lo}) - \mu_2(E_{lo})}.$$

Note that w_{1/S_A}^* is not dependent on D and d . Hence, for this choice of weight, there will be no contrast between tissue 1 and 2 whatever the thickness of the two tissues are, which in this case means that object 2 will not be visible at all. At the same time, tissue 3 will still have contrast relative to tissue 1 and 2, making it detectable. As mentioned, tissue 1, 2 and 3 could be adipose, glandular and tumor tissue respectively. However, in reality the case is of course more complicated. For example, the beam is not mono-energetic, but contains an entire spectrum of energies. This unfortunately makes it impossible to get complete contrast cancelation for all thicknesses of glandular tissue.

3.2.3 The Tissue Phantom

X-rays interact with matter in the following type of interactions: photoelectric effect, Compton scattering, Rayleigh scattering, and pair and triplet production. In mammography, the energies are too low for pair or triplet production, and Rayleigh scattering has only a negligible effect. Since the material and energy dependencies of the cross section are approximately decoupled, the linear attenuation for a material can be written as [22, 23]

$$\mu_m(E) \simeq c_\tau(m)\tau(E) + c_\sigma(m)\sigma(E), \quad (3.6)$$

where $\tau(E)$ and $\sigma(E)$ denote the energy dependencies of photoelectric absorption and Compton scattering respectively, and $c_\tau(m)$ and $c_\sigma(m)$ are material-specific constants. $\tau(E) \simeq E^{-3}$ for energies above the highest atomic binding energy and $\sigma(E)$ is given by the Klein-Nishina formula. Because of this, it is possible to express the linear attenuation of a specific material in terms of the linear attenuation of two other materials,

$$\mu_m(E) \simeq a_1(m)\mu_1(E) + a_2(m)\mu_2(E). \quad (3.7)$$

The imaging phantom in the present study was designed based on this. The aluminum alloy Al-6082 (notation according to the International Alloy Designation System) and ultra high molecular weight polyethylene were combined in different compositions to simulate breast tissue with a total thickness of 4.5 cm. Figure 3.3 shows a CAD model of the phantom, and as can be seen in Fig. 3.4 Left, the different tissues simulated include healthy tissue with glandularity (fraction of glandular tissue) ranging from 0 to 1 in steps of 0.1, and tumors of different thicknesses embedded in tissue with glandularity 0, 0.5 and 1. Figure 3.4 Center shows the corresponding thickness of aluminum and polyethylene.

Figure 3.3: CAD model of the phantom

50 0.5	0 0.5	0 1	0 2	0 4	4.3588 0.1144	4.3332 0.0487	4.3424 0.0671	4.3606 0.1038	4.3972 0.1772
50 1	50 0	0 0	10 0	20 0	4.3647 0.1246	4.3528 0.1043	4.3241 0.0304	4.3298 0.0452	4.3356 0.0600
50 2	30 0	40 0	60 0	70 0	4.3766 0.1449	4.3413 0.0747	4.3471 0.0895	4.3586 0.1191	4.3643 0.1339
50 3	80 0	90 0	100 0	50 0	4.3885 0.1651	4.3700 0.1487	4.3758 0.1634	4.3815 0.1782	4.3528 0.1043
50 4	100 0.5	100 1	100 2	100 4	4.4004 0.1854	4.3843 0.1801	4.3870 0.1821	4.3926 0.1859	4.4036 0.1936

Figure 3.4: **Left:** Description of what tissue the phantom simulates. The numbers to the top and bottom of each square represents glandularity in percent and tumor thickness in cm, respectively. **Center:** Thickness in cm of polyethylene and aluminum (numbers on the top and bottom, respectively) corresponding to the tissue shown to the left. **Right:** X-ray image of the phantom.

Each of the 25 fields of the phantom is $3 \times 3 \text{ cm}^2$. A non-energy-resolved x-ray image of the phantom is shown in Fig. 3.4 Right.

With all μ_i in Eq. (3.7) known for various energies, the coefficients a_i were determined by minimizing the difference between the left and right sides of the equation for these energies. Numerical values for attenuations coefficients for glandular, adipose and cancerous tissues were taken from Ref. [24]. The thicknesses of aluminum and polyethylene, d_a and d_p respectively, corresponding to a thickness d_t of a certain tissue, are then given by the following equation

$$\mu_t d_t \simeq (a_a \mu_a + a_p \mu_p) d_t = \mu_a (a_a d_t) + \mu_p (a_p d_t) \equiv \mu_a d_a + \mu_p d_p. \quad (3.8)$$

3.2.4 Imaging Performance Metrics

To quantify the degree of suppression of the anatomical background in DES, the following signal-difference-to-noise-ratio (SDNR) was defined

$$\text{SDNR}_A = \frac{|\bar{I}_t(g) - \bar{I}_n(g)|}{\sigma_A}, \quad (3.9)$$

where $\bar{I}_t(g)$ and $\bar{I}_n(g)$ denote the mean signal from normal tissue with a glandular fraction g , with and without an embedded tumor, respectively. σ_A is the anatomical noise and is defined as the standard deviation of $\bar{I}_n(g)$ over a range of g . The SDNR_A describes, without taking shape or resolution into regard, how well the target can be distinguished from the background. Because this metric uses only average intensities, taken over an almost 9 cm^2 large area, the effect of quantum noise is eliminated.

It is, however, important to take quantum noise into consideration, especially when it comes to detection of smaller targets. Therefore, a quantum SDNR was also introduced,

$$\text{SDNR}_Q = \frac{|\bar{I}_t(g) - \bar{I}_n(g)|}{\sigma_n(g)}, \quad (3.10)$$

where $\sigma_n(g)$ is the quantum noise in the signal coming from normal tissue with glandular fraction g . In the measurement, $\sigma_n(g)$ is computed as the standard deviation of $I_n(g)$, while in the simulations performed, it was calculated simply as the

$$\sigma_n(g) = \sqrt{w^2 \bar{n}_{lo,n}(g) + \bar{n}_{hi,n}(g)}, \quad (3.11)$$

where w is the weight factor. Unlike the anatomical SDNR, the quantum SDNR is dependent on exposure, and is proportional to the square root of the number of photons.

For the computation of the metrics above, the dual-energy image I' in Eq. (3.2) was used.

3.3 Results and Discussion

The choice of weight factor is a crucial point in spectral imaging. By performing a scan of w , the optimal performance according to a given metric can be obtained. The left graph in Fig. 3.5 shows SDNR_A versus w for tumors of thickness 1 and 2 cm embedded in tissue with a glandularity of 0.5. This graph highlights one of the challenges in dual-energy subtraction; with only a small change in w , the SDNR can go from a minimum to a maximum. The improvement in SDNR_A with DES compared to non-energy-resolved imaging ($w = 1$) is 97% for the 2 cm tumor embedded in tissue with a glandularity of 0.5.

Figure 3.5: SDNR_A (left) and SDNR_Q (right) versus weight factor for tumors of thickness 1 and 2 cm embedded in equal fractions of glandular and adipose tissue.

Figure 3.5 also shows SDNR_Q for the same cases. For a w that maximizes the SDNR_A , the SDNR_Q is small and close to its minimum. This clearly demonstrates the trade-off between reduction in anatomical noise and increase in quantum noise. We also note that for $w \approx 2$ the SDNR_Q has a maximum, with a 7% improvement compared to the non-energy resolved case, corresponding to $w = 1$. Simulations yielded an improvement in the order of 1%. The reason for this discrepancy is not known at this point.

Instead of having a constant weight factor, w could alternatively be chosen to be a polynomial in the number of counts in the low- and high-energy bins. A preliminary investigation showed that further improvement of the SDNR_A could be achieved by minimizing σ_A with respect to the coefficients in the polynomial. This was, however, not further investigated.

Figure 3.6 Left shows a montage of the image shown in Fig. 3.4 Right. Fields with an area corresponding to a 2-cm-diameter circle were cut out and put together. Square (2,2), (4,2) and (3,4), where the indices denote rows and columns respectively, correspond to tumors of thickness 0.5, 1 and 2 cm embedded in normal tissue with a glandular fraction of 0.5. The rest of the squares correspond to healthy tissue with glandularity ranging from 0.2 to 0.8. It is impossible to distinguish the tumors from normal tissue in the non-energy-resolved image, since their intensities lie in the range of the normal tissue.

Figure 3.6: Images of the tissue phantom. **Left:** Non-energy resolved absorption image. **Center:** Low-pass filtered DES image without contrast adjustment. **Right:** Low-pass filtered DES image with contrast adjustment.

Figure 3.6 Center shows the DES image. Because w is chosen to minimize the anatomical background, the SDNR_Q is low. This is compensated for by low-pass filtering the image. The tumors are now conspicuous, especially after applying a contrast window as shown in Fig. 3.6 Right. This clearly illustrates a case where DES could be useful.

However, as can be seen in Fig. 3.7, DES can not always uniquely distinguish tumors from healthy tissue. The circles and squares represent the mean image signal from tissue with and without embedded tumors, respectively. The tumor thickness varies from 0.5 to 4 cm, and they are embedded in tissue with a glandularity of 0, 0.5 and 1 (cf. Fig. 3.4 Left). By including the entire range of glandularity, the tumors in the case above lies in the same image value range as the background. The situation is similar for tumors embedded in only adipose and glandular tissue.

The agreement between model and measurements is investigated in Fig. 3.8, which shows the intensities in the low- and high-energy bin for various tumor thicknesses and tissue with different glandularity. All intensities have been mapped to PMMA thickness, which is approximately equivalent to taking the logarithm. The model was found to accurately predict the measured quantities.

As can be seen in the right graph in Fig. 3.8, the high-energy image displays a larger value than the low-energy image for adipose tissue, while for glandular tissue it is the other way around. This illustrates the energy dependencies of the linear attenuation coefficients of different materials.

Figure 3.7: Mean image values of all the different fields of the phantom. **Left:** Non-energy resolved absorption image. **Right:** DES image minimizing anatomical background

Figure 3.8: Non-energy-resolved imaging: mean image values for different types of tissue compositions.

The errors due to uncertainties in the thickness of the aluminum and polyethylene was estimated to be small. The signals from the two fields that were designed to be identical (corresponding to tissue with glandularity 0.5) differed by 1%.

Furthermore, the x-ray radiating through the phantom at an angle θ to the z -direction (Fig. 3.1) will go through a factor $(\cos \theta)^{-1}$ longer distance in the phantom. In addition to the heel effect, this will result in further uncertainties. To quantify this, the mean signal from the different fields in the phantom was compared between two images, where the phantom was rotated 180° in the second image. The maximal deviation was found to be less than 2%. However, this error was reduced by using data only from the top area (cf. Fig. 3.4) in the images, where the radiation is close to perpendicular to the phantom surface. This also minimizes uncertainties due to the heel effect.

3.4 Conclusions

Compared to non-energy-resolved imaging, unenhanced dual-energy subtraction was experimentally shown to improve the SDNR in cases where the anatomical noise dominates. When quantum noise is the limiting factor, energy weighting is advantageous, and it was also experimentally shown that this scheme can improve detectability. Furthermore, the measurements validated the computer model for unenhanced spectral imaging.

Chapter 4

Spectral Tomosynthesis

This chapter presents an evaluation of the photon-counting spectral breast tomosynthesis system developed within the EU-funded HighReX project [25, 26]. Using an ideal-observer detectability index incorporating anatomical noise as figure of merit, tomosynthesis, spectral imaging, and the combination of both are compared. Predictions of signal and noise transfer through the system are verified by 3D measurements of the MTF and NPS.

4.1 Introduction

Tomosynthesis spans the continuum from projection imaging (0° angular range) to cone beam computed tomography (180° angular range) [11–13]. The anatomical background is reduced by increasing the angular range, but this also results in increased quantum noise (or patient dose). The angular range thus has to be optimized with respect to the imaging task considered.

The combination of spectral imaging and tomosynthesis has been presented in the past [25, 27], but the benefit of such an approach remains somewhat unclear. This study is a first step toward a quantitative analysis of the combination. In particular, both modalities aim at reducing anatomical noise at similar trade-offs with quantum noise, and the question arises whether both are needed.

In the present study, a computer model was developed for characterizing the 3D MTF and NPS of the approximately linear system. A task-dependent detectability index incorporating anatomical noise was used as a figure of merit to compare non-energy-resolved absorption imaging with spectral imaging.

4.2 Materials and Methods

4.2.1 Description of the System

Figure 4.1 Left shows a photograph of the spectral tomosynthesis system. It is a modification of the Sectra MicroDose Mammography 2D imaging system. In the 2D system, the arm is rotated around the x-ray source (cf. Fig. 3.1), while in the tomosynthesis system the center of rotation is located below the detector, as shown in Fig. 4.1 Right. By a scanning motion

Figure 4.1: Photograph and schematic of the spectral tomosynthesis system. Photo courtesy of Sectra Mamea AB.

across the breast, 21 projections are acquired simultaneously. The angular coverage of the system is 11° .

The tomosynthesis reconstruction is based on the convex algorithm introduced by Lange [28], which is an iterative method, similar to expectation maximization. Iterative methods have proven efficient for limited data reconstructions, and the intense calculations are no longer considered a problem.

4.2.2 System Modeling

Linear-systems theory has been successfully used in the past to characterize tomosynthesis systems [11–15] and spectral imaging systems [8, 9, 19]. In this work, a model for signal and noise transfer in tomosynthesis was developed and combined with the spectral imaging model presented in the previous chapter. The tomosynthesis model is summarized below, but the reader is referred to Refs. [13] and [15] for a more comprehensive description.

Signal and Noise Transfer in Tomosynthesis

A necessary condition for linear-systems theory to be applicable to tomosynthesis is that the reconstruction algorithm is linear, which is true for filtered back projection (FBP). FBP is directly based on the Fourier slice theorem, which states that the Fourier transform of a projection of an object is equal to the parallel slice through the origin of the Fourier transform of the object. Hence, by acquiring projections from different angles and putting them together accordingly, the Fourier space is sampled. By taking the inverse Fourier transform, the reconstruction of the object is obtained. Since the angular range is limited in tomosynthesis, the Fourier space is only partially filled and an accurate reconstruction of the attenuation coefficients is not possible.

Because of its simplicity and linearity, FBP is used to model the tomosynthesis system, although, in reality, the tomosynthesis system uses a non-linear (iterative) reconstruction

algorithm. The Fourier slice theorem is, however, still valid, and the approximative agreement was regarded sufficient to predict trends. In addition, it is shown below that close agreement can be accomplished by tuning a few linear filter parameters of the FBP algorithm (A and B in Eqs. (4.1) and (4.2)).

The MTF and NPS from the spectral imaging model [9, 19, 20] were propagated through four different stages associated with filtered back projection:

1. Since the measured data is on the form $I = I_0 \exp(-\int \mu(z)dz)$ and tomography aims at reconstructing the linear attenuation coefficients μ of the object, the projection data is transformed to $P = -\ln(I/I_0) = \int \mu(z)dz$. The first stage is hence a logarithmic transform, which in a linear approximation equals normalization with the average pixel intensity [15].
2. Reconstruction filters associated with FBP reconstruction are applied. These filters include ramp, interpolation and apodization filters, which change the signal and noise in a deterministic way. The ramp filter can be thought of as a weighting function compensating for the fact that the Fourier space is more densely sampled closer to the origin. It is only applied in the scan direction (henceforth denoted the y' -direction) and is given by

$$F_R(f_{y'}) = f_{y'}^A. \quad (4.1)$$

As noted above, A can be used to tune the linear FBP model to be comparable to iteratively reconstructed measurements on the system. The model predictions, except for comparison to MTF and NPS measurements, were, however, done in the FBP regime with $A = 1$.

Interpolation is necessary in the reconstruction because the projection signal needs to be known at any location on the detector, and not only the pixel centers [29]. Bilinear interpolation is equivalent to convolving a unit area triangle function in the spatial domain, which corresponds to multiplication with a squared sinc-function in the frequency domain. The interpolation filter is applied in both directions (x and y'),

$$F_I(f_x, f_{y'}) = \text{sinc}^2(a_x f_x B) \times \text{sinc}^2(a_y f_{y'} B), \quad (4.2)$$

where a denotes the pixel side. B is the second tuning parameter that was used for comparison to measurements. Again, $B = 1$ in the FBP regime.

To reduce aliasing and high-frequency noise, which is amplified by the ramp filter, an apodization filter is applied in the y' -direction. A Hann window was used for this purpose:

$$F_W(f_{y'}) = 0.5(1 + \cos(b f_{y'})), \quad (4.3)$$

where b is a window parameter, set to π/f_{Ny} in this study, with f_{Ny} being the Nyquist frequency. The MTF and NPS, denoted by T and S respectively, at the end of stage 2 are given by

$$T_{\text{proj}} = F_R \times F_I \times F_W \times \frac{T_{2D}}{k} \quad (4.4)$$

$$S_{\text{proj}} = F_R^2 \times F_I^2 \times F_W^2 \times \frac{S_{2D}}{k^2}, \quad (4.5)$$

where T_{2D} and S_{2D} are the outputs from the 2D spectral detector model and k is the average pixel intensity.

3. In the back projection stage, T_{proj} and S_{proj} are projected into 3D-space according to the Fourier slice theorem, which can be represented using the Dirac delta-function [15]:

$$T_{3D} = \frac{N}{\theta f_{y'}} \sum_{i=1}^N \delta(f_y \sin \theta_i - f_z \cos \theta_i) \times T_{\text{proj}} \quad (4.6)$$

$$S_{3D} = \frac{N}{\theta f_{y'}} \sum_{i=1}^N \delta(f_y \sin \theta_i - f_z \cos \theta_i) \times S_{\text{proj}}, \quad (4.7)$$

where N is the number of projections, θ is the angular range, and θ_i is the projection angle. The factor $N/\theta f_{y'}$ is a normalization factor needed when converting from polar coordinates to Cartesian coordinates [15]. With a limited angular range as in tomosynthesis, only a wedge-shaped region is filled in Fourier space, as opposed to CT where the entire Fourier space is sampled.

4. 3D sampling is the last stage, which introduces aliasing.

Finally, to obtain the NPS and MTF in a tomosynthesis slice, an integration over f_z within the Nyquist region was carried out. As noted in Ref. [15], this is equivalent to an integration over all f_z without aliasing in the z -direction. The magnitudes of S_Q and S_A were taken to be proportional and inversely proportional, respectively, to θ , at constant signal. The slice thickness was taken to be inversely proportional to θ and was tuned to 1 mm for $\theta = 40^\circ$.

Ideal-Observer Detectability

A task-dependent ideal-observer detectability index was used as a figure of merit. In the 2D case, i.e. conventional projection imaging, it is given by Eq. (2.9),

$$d_{2D}^{\prime 2} = \int \int \frac{T^2(f_x, f_y) \times (\Delta s)^2 \times F^2(f_x, f_y)}{T^2(f_x, f_y) S_A(f_x, f_y) + S_Q(f_x, f_y)} df_x df_y. \quad (4.8)$$

In this study, detection of tumors modeled by Gaussian functions are considered, which results also in a Gaussian task function, emphasizing low frequencies.

In tomosynthesis, the detectability calculated in a slice was used for comparison. It is given by [13]

$$d_{\text{slice}}^{\prime 2} = \int \int \frac{|\int T(f_x, f_y, f_z) \times \Delta s \times F(f_x, f_y, f_z) df_z|^2}{\int (T^2(f_x, f_y, f_z) S_A(f_x, f_y, f_z) + S_Q(f_x, f_y, f_z)) df_z} df_x df_y, \quad (4.9)$$

where the integral over f_z is carried out before division.

4.2.3 Measurements

The measurements in this study were performed on a non-energy-resolved tomosynthesis system, similar to the one used in Ref. [25]. The $50 \times 50 \mu\text{m}^2$ detector pixels were binned into $100 \times 100 \mu\text{m}^2$ pixels. These measurement were used to validate the model of the tomosynthesis system. In addition, clinical images have been acquired with a spectral tomosynthesis system.

NPS and MTF

The NPS was measured in flat-field images of a 4 cm PMMA slab. 256 128×128 pixel large regions of interest were generated from a set of four images. The NPS was then calculated as the ensemble average of the squared fast Fourier transform of the difference in image signal from the mean in each region, according to Eq. (2.5).

The PSF in the y - z -plane was measured with a 50 μm thin tungsten wire slanted in the plane at 12.4° to the y -axis. The 2D PSF, which is pre-sampled in z but not in y , was calculated from a single slice in the reconstructed volume with the wire angle as input [14, 30]. The PSF in the x -direction is virtually independent of the y - z -resolution and was measured with the same wire, but slanted in the x - y -plane for over-sampling. The measurement was somewhat complicated by the strong edge enhancement in the y -direction; the wire is erroneously enhanced by its y -component. This problem was overcome by using a very slight angle and over-sample at well separated points on the wire. MTFs were calculated as the magnitude of the Fourier transforms of the 1D and 2D PSFs.

Spectral Tomosynthesis: Clinical Images

Clinical trials have been conducted with a spectral tomosynthesis system during 2010 at Charité University Hospital, Berlin, Germany. Samples of the acquired images are shown in this study to illustrate the capabilities of the system.

4.3 Results and Discussion

4.3.1 Measurements

NPS and MTF

As described above, the parameters A and B were tuned to fit the theoretical NPS to the measured quantity. The NPS was used for the fitting because the measurement was regarded less prone to error than the MTF measurement. An additional normalization factor was introduced for both quantities to adjust the magnitude.

Figure 4.2 Left shows the measured in-depth (y - z -plane) NPS. It displays streaks resulting from the angular separation between the projections. As mentioned above, by integrating the 3D NPS over the z -direction, the slice or in-plane (x - y -plane) NPS is acquired, which is shown in Fig. 4.2 Center. By setting $A = 0.5$ and $B = 2.5$, the model was successfully tuned to fit the NPS, as can be seen in Fig. 4.2 Right and Fig. 4.3 Left. Also the MTF exhibits reasonably good agreement (cf. Fig. 4.3 Right). $A = 0.5$ results in less suppression of low frequencies. Modifications of the ramp filter in order to preserve low-frequency information have been used previously [31]. $B = 2.5$ corresponds to interpolation with four to five neighboring points to approximate the value in a given point, which would reduce noise and spatial resolution.

Spectral Tomosynthesis: Clinical Images

Figure 4.4 shows examples of tomosynthesis breast images acquired with the system. The left image is a non-energy-resolved absorption image, and to the right a thresholded dual-

Figure 4.2: **Left:** Measured in-depth NPS. **Center:** Measured in-plane NPS. **Right:** Theoretical in-plane NPS

Figure 4.3: **Left:** Measured and theoretical NPS. **Right:** Measured and theoretical MTF.

energy subtracted spectral image, colored in purple and pink, has been overlaid on the absorption image so that a tumor clearly stands out. Iodine was used for contrast enhancement.

4.3.2 System Modeling

Figure 4.5 plots detectability index (d') of a contrast-enhanced tumor versus angular extent (θ) for spectral and non-energy-resolved 2D imaging ($\theta = 0^\circ$) and tomosynthesis. The total dose for the examination was kept constant and equal to 1 mGy. Contrast enhancement with 3 mg/cm^3 iodine and high anatomical background was assumed. The standard deviation of the Gaussian function was set to 1 cm to model a clinical case similar to the one presented in

Figure 4.4: Tomosynthesis images with contrast enhancement. **Left:** Non-energy-resolved image. **Right:** Spectral image (colored in purple and pink) overlaid on the non-energy-resolved image. Image courtesy of Felix Diekmann, Charité University Hospital. Color image available online.

Figure 4.5: Detectability index of a contrast-enhanced tumor versus total angular extent for spectral and non-energy-resolved tomosynthesis. d' at $\theta = 11^\circ$ should be compared with the clinical case in Fig. 4.4

Fig. 4.4. The model predicted that spectral tomosynthesis may improve tumor detectability compared to non-energy-resolved tomosynthesis, which is in agreement with the clinical results. Since the model at this point includes some simplifications, for example regarding the dependence of S_A and S_Q on θ , the result presented in Fig. 4.5 should be considered qualitative. Because of this, a complete comparison of all the modalities, with different detection tasks, anatomical noise magnitude and angular range, is not presented at this stage, but is part of ongoing research.

4.4 Conclusions

It was possible to tune the linear FBP-based model to agree well with measurements of both MTF and NPS. It is clear that the model cannot quantitatively predict results of the iterative reconstruction without tuning, but trends predicted by the model are expected to be fairly accurate and applicable to the system.

For detection of a contrast-enhanced tumor in a breast with high anatomical background, the optimum performance for spectral tomosynthesis was found at a tomo-angle of 10 degrees. The improvement was in the order of a factor 10 compared to non-energy-resolved tomosynthesis with the same angular extent. This was supported by clinical results.

Potential benefits of spectral tomosynthesis may also include localization of contrast-enhanced tumors in the depth direction and better accuracy of tissue discrimination tasks, which will be subject of future studies.

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