Estimating Breast Thickness for Dual-Energy Subtraction in Contrast-Enhanced Digital Mammography: A Theoretical Model

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Abstract. Dual-energy contrast-enhanced digital mammography (DE CE-DM) images the perfusion and vasculature of the breast using an iodinated contrast agent. High-energy (HE) and low-energy (LE) images of the breast are acquired; the DE image is obtained by a weighted logarithmic subtraction of the image pair. We hypothesized that the optimal DE subtraction weighting factor, w, is dependent on three parameters: breast thickness, kV, and filter material. We simulated the attenuation of x-rays through breasts of thicknesses ranging from 0.5 to 10 cm using different filter and kV combinations. The glandularity of the phantom for a given thickness was varied using different combinations of adipose and glandular tissues. We calculated the logarithm of the LE and HE signal intensities. For a given kV-filter pair, the signals decrease with increasing tissue thickness and glandularity. The DE weighting factor is thickness-dependent, and it decreases with increasing energy difference between the LE-HE kV pairs. These results facilitate the subtraction of tissue in the periphery of the breast, and aid in discriminating between contrast agent uptake in glandular tissue and subtraction artefacts.

Keywords: Breast · Dual-energy · Contrast-enhanced · Digital mammography · Glandularity · Software simulation

1 Introduction

Contrast-enhanced breast imaging is motivated by the observation that angiogenesis accompanies the development of cancer. Contrast-enhanced MRI (CE-MRI) is the current gold standard for imaging breast cancer perfusion and the characterization of lesions in the diagnosis of breast cancer. This imaging modality is also used to screen women who have a high risk of developing breast cancer. Although CE-MRI provides important information about the vasculature of breast lesions, it suffers from low spatial resolution when compared to conventional digital mammography (DM). For instance, microcalcifications are better visualized in DM than in CE-MRI.

Contrast-enhanced digital mammography (CE-DM) has emerged as an alternative to CE-MRI. An iodinated contrast agent is used in CE-DM to image the perfusion and

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vasculature of the breast. CE-DM has great potential to improve the detection and diagnosis of breast cancer by combining morphologic and functional information on vascular kinetics in a single examination. It has the ability to acquire functional characteristics of breast lesions at a spatial resolution that is comparable to DM. Furthermore, CE-DM allows us to quantitatively assess the linear relationship between the attenuation coefficient and the concentration of contrast agent uptake. Contrast uptake by breast tissue is made more evident by dual-energy (DE) subtraction. In DE x-ray breast imaging, low-energy (LE) and high-energy (HE) images of the breast are acquired. The x-ray energies are chosen so that the k-edge of the contrast agent is in the range spanned by the LE and HE x-ray spectra, allowing us to distinguish between the linear attenuation coefficients of the soft tissue and contrast agent signals.

The goal of DE subtraction is to cancel the signal from the background breast tissue and to increase enhancement conspicuity. In addition, DE subtraction minimizes patient motion because the HE and LE image pairs are acquired almost simultaneously. The DE image is obtained by performing a weighted difference of the logarithms of the LE and HE images. The DE signal intensity S^{DE} is expressed as

$$S^{DE} = \ln(S^{HE}) - w * \ln(S^{LE}), \tag{1}$$

where w is the DE weighting factor, S^{HE} is the signal intensity of the HE image, and S^{LE} is the signal intensity of the LE image. The weighting factor, w, is calculated to eliminate the dependence of the DE signal on the glandular-adipose signal of the breast tissue, and it is expressed as

$$w = \frac{\mu_a^{HE} - \mu_g^{HE}}{\mu_a^{LE} - \mu_g^{LE}} = \frac{\ln(S_a^{HE}) - \ln(S_g^{HE})}{\ln(S_a^{LE}) - \ln(S_g^{LE})}, \tag{2}$$

where μ is the linear attenuation coefficient and the subscripts a and g represent adipose and glandular tissues, respectively. This is based on the work of Karunamuni and Maidment [1].

Current methods for DE subtraction do not consider compressed breast thickness, and a constant weighting factor is applied to the entire image. In our previous work, we developed a method for determining breast thickness and composition in DE CE-DM [2]. The motivation for our work arises from the difficulty in resolving contrast uptake at the boundaries of the breast in DE subtraction. A number of studies have noted the presence of subtraction artefacts in DE CE-DM [3, 4]. Yagil *et al.* [4] classify these artefacts into four categories: rim, ripple, axillary line, and skin-line artefacts.

We hypothesize that the optimal DE weighting factor is dependent on three different parameters: breast thickness, kV combination, and filter combination. Therefore, weighting factors near the periphery of the breast, where the breast is thinner, should be different from those in the centre. Methods for quantification of breast composition using DE mammography have been explored by Ducote and Molloi [5] and Laidevant *et al.* [6]. However, these methods require the use of a calibration phantom and do not quantitatively determine the breast thickness. By quantifying the breast thickness and composition as a function of position, we can optimize our DE subtraction by finding the optimal weighting factor at each pixel location.

2 Methods

Polyenergetic x-ray spectra were generated using simulation software developed by Boone and Seibert [7]. The software simulates x-ray spectra with a tungsten anode at 1 keV intervals using interpolating polynomials. X-ray energies were chosen so that the k-edge of iodine (33.2 keV) was in the range spanned by the LE and HE x-ray spectra. The kV, filter material, and filter thickness parameters used reflect those available on the prototype DE Hologic Selenia Dimensions imaging system (Table 1).

Table 1. Summary of parameters used in software simulation.

	Energy of Spectra (kV)	Filter	
		Material	Thickness (μm)
Low-Energy	25–35 kV	Aluminum	700
		Rhodium	50
		Silver	50
High-Energy	40–49 kV	Copper	200
		Copper	300

Breast tissue was modelled by simulating phantoms consisting of a uniform composition of glandular and adipose tissues. The thickness of the phantoms ranged from 0.5 to 10 cm, in 0.5 cm increments. The glandular-adipose composition of the phantom was varied in 10 % increments from 0 % glandularity to 100 % glandularity for a given thickness (Fig. 1).

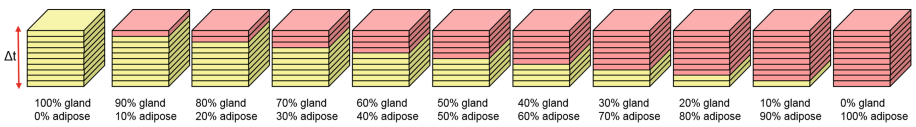

Fig. 1. Example of a tissue phantom composed of adipose (red) and glandular (yellow) tissues (Colour figure online).

Given the incident number of photons, N_0, from an x-ray beam, the number of photons transmitted through a phantom, N_{ph}, at a specific energy bin, E, is given by the Beer-Lambert law as

$$N_{ph}(E) = N_0(E)e^{-(\mu_g m_g + \mu_a m_a)t_{ph}}, \tag{3}$$

where t_{ph} is the phantom thickness, μ is the linear attenuation coefficient, m is the percent tissue composition, and the subscripts a and g represent adipose tissue and glandular tissue, respectively. The glandular and adipose tissue compositions are related by

$$m_g + m_a = 1. \tag{4}$$

An energy-integrating selenium detector was modelled in our simulation, and the signal intensity of the phantom, S_{ph}, is determined by

$$S_{ph} = \sum^{E_{\max}} N_{ph}(E) * E * e^{-\mu_{Se} t_{Se}}, \quad (5)$$

where E_{max} is equal to the simulated tube potential, μ_{Se} is the linear attenuation coefficient of selenium, and t_{Se} = 0.5 mm is the thickness of the selenium. The DE signal intensity for each phantom was determined using the DE subtraction method detailed in Sect. 1.

3 Results and Discussion

The HE and LE spectra were generated using software simulation; the spectra were normalized by the mAs. A total of 145,200 phantoms were simulated in our study. Results from the tissue phantom simulation were plotted parametrically. The mean logarithmic HE intensity values, ln S^{HE}, were plotted against the mean logarithmic LE intensity values, ln S^{LE} (Fig. 2). The mean logarithmic LE and HE signal intensities vary with phantom thickness and glandularity. For a given kV-filter pair, the mean logarithmic LE and HE signals decrease with increasing tissue thickness, and they also decrease linearly with increasing glandularity for a given thickness. A linear fit was modelled for each thickness. The mean r^2 for the linear fits is 0.999, indicating that a linear model is appropriate. It is important to note that the DE weighting factor, w, is represented graphically as the slope, $\frac{\Delta(\ln S^{HE})}{\Delta(\ln S^{LE})}$, of the linear fit. Therefore, it is relevant to calculate the weighting factor as a function of breast thickness.

It is shown upon closer inspection that for a given kV-filter pair, the slopes of these linear fits are not parallel. The weighting factor, w, was plotted three-dimensionally as a function of LE and HE (Fig. 3). Each surface represents a constant tissue thickness. The weighting factor changes with tissue thickness and kV pair. We previously showed that DE subtraction has the purpose of projecting a two-dimensional LE-HE signal pair down to a single value, and each thickness has a distinct DE signal [2]. The DE signal is unique for each thickness because DE subtraction intrinsically encodes breast thickness information when using the common weighting scheme designed to eliminate the signal between glandular and adipose tissues.

It is worth noting that there is a region of convergence between the different thickness surfaces. This is further illustrated in Fig. 4. The behaviour of the thickness surfaces can be divided into three different regions. The two surfaces represent tissues of different thickness; the red surface represents a thicker breast than the blue surface. Region I represents the situation in which the thickness surfaces converge. This indicates that the linear fits as a function of breast thickness of ln S^{HE} versus ln S^{LE} are parallel. Therefore, the weighting factor is constant for LE-HE kV pairs in this region. Region II represents the situation in which the fits converge to the left. Thus, the weighting factor decreases with increasing thickness. Region III represents the situation in which the fits converge to the right. This indicates that the weighting factor increases with increasing thickness. DE subtraction is simplified in Region I as only a single

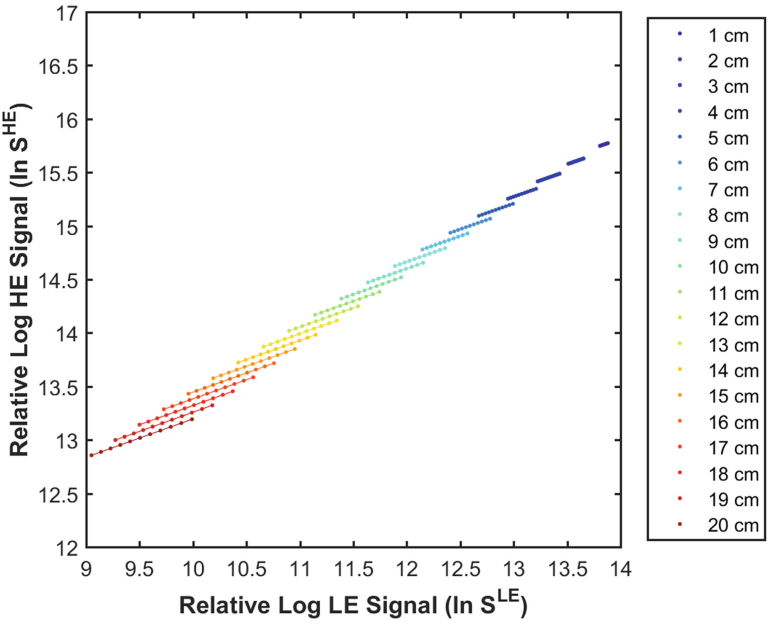

Fig. 2. Signal intensities for simulated breast tissue phantoms at thicknesses from 0.5 to 10 cm. Results are shown for a 30 kV/Rh 50 μm (LE) and 49 kV/Cu 300 μm (HE) pair (Colour figure online).

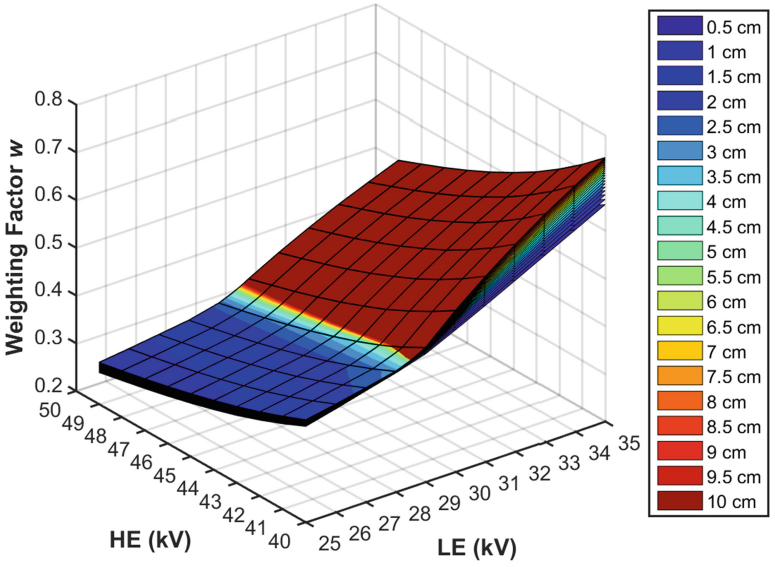

Fig. 3. DE weighting factor, *w*, as a function of HE and LE at a constant thickness. Results are shown for a 30 kV/Rh 50 μm (LE) and 49 kV/Cu 300 μm (HE) pair (Colour figure online).

w value is needed. However, a residual signal from the variations in breast thickness is still preserved. By contrast, regions II and III require a different weighting factor and a thickness correction as a function of thickness.

We then determined the range of DE values spanned by the linear fits of the thickest and thinnest phantoms. To calculate this value, we first located the point along the 5 cm linear fit that represented 50 % adipose/50 % glandular tissue. Next, we found the normal to the line at that point, and measured the distance between where the normal intersected the 0.5 cm and 10 cm lines.

The DE range was plotted as a function of LE and HE (Fig. 5). The range increases with increases in the energy difference between the LE- HE kV pairs. A maximal range value is desired for DE subtraction because this facilitates our ability to distinguish between different tissue thicknesses. This corresponds to a minimal DE weighting factor, as seen in Fig. 3.

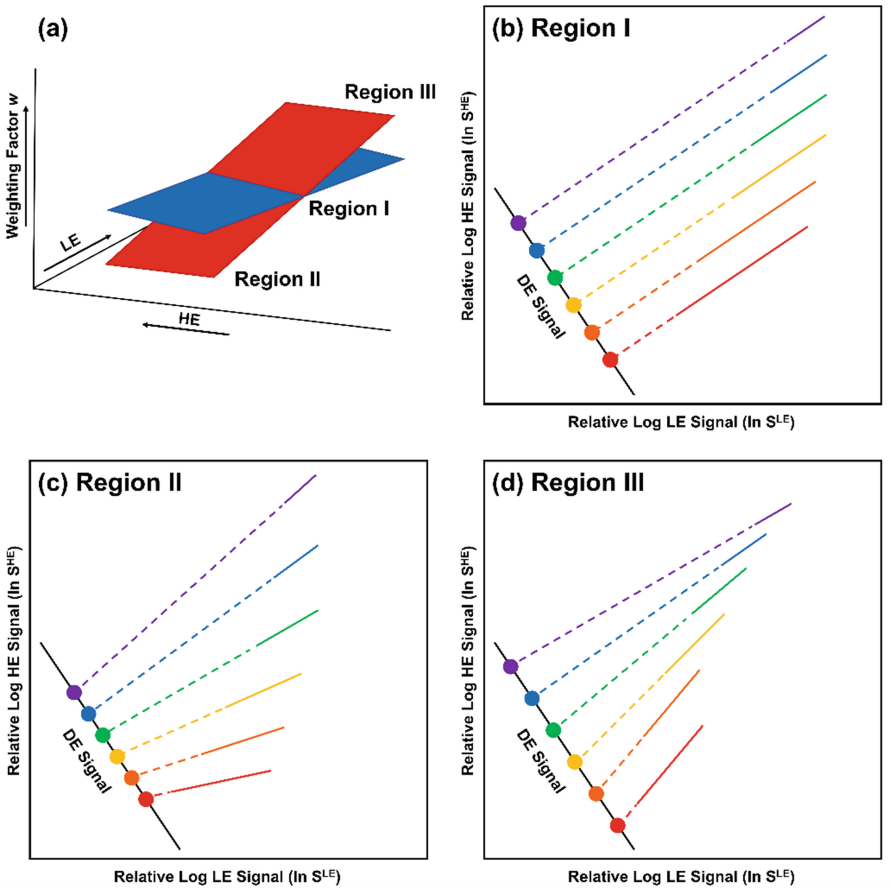

Fig. 4. (a) Illustration of the possible behaviours of signal intensity pairs projected onto DE signal space (black line) for a given kV pair and filter pair combination: (b) parallel, (c) converging, and (d) diverging (Colour figure online).

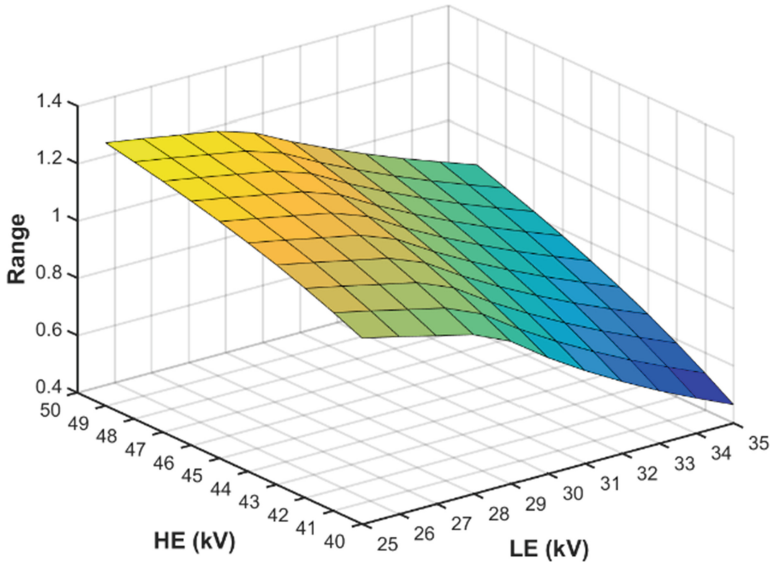

Fig. 5. Range as a function of HE and LE. Results are shown for a 30 kV/Rh 50 μm (LE) and 49 kV/Cu 300 μm (HE) pair (Colour figure online).

Upon closer inspection of the range, it can be shown that there is a set of optimal energy differences for a LE-HE kV pair. We plotted the range versus energy difference at a constant HE, and it can be seen that there is a region where the range value sharply increases. This set of kV differences corresponds to the same region where the range increases slowly in the plot of range versus energy difference at a constant LE. These results indicate that for a given HE or LE value, there is an optimal corresponding LE or HE value in order to determine tissue thickness (Fig. 6).

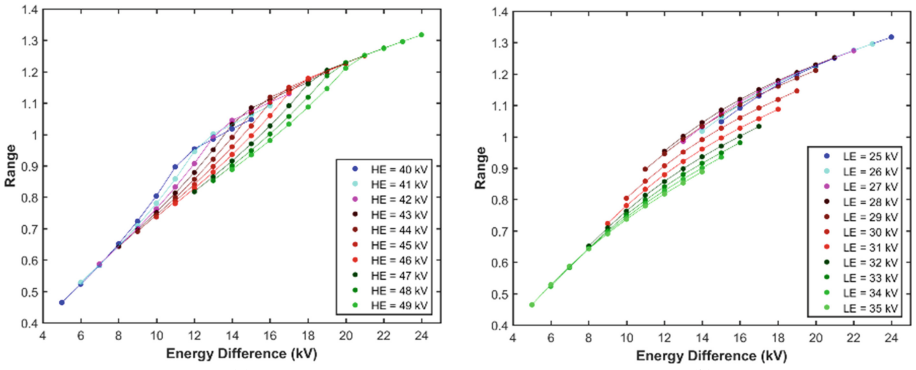

Fig. 6. Range as a function of energy difference at (a) constant HE and (b) constant LE. Results are shown for a 30 kV/Rh 50 μm (LE) and 49 kV/Cu 300 μm (HE) pair (Colour figure online).

4 Conclusions

We have developed a framework to determine breast tissue thickness and composition quantitatively in DE CE-DM. We have shown that breast thickness and composition can be predicted from the linear relationship between LE and HE signal intensities. This is possible because each tissue thickness has a distinct DE signal. Therefore, breast thickness is intrinsically encoded in DE subtraction when using the common weighting scheme to eliminate the signal between glandular and adipose tissues. This has implications for the weighting factor used in DE subtraction for a given thickness. We have also shown that the weighting factor, w, changes with thickness, kV of the spectra, and filter combination. In addition, we have shown that for a given HE or LE value, there is a corresponding LE or HE value that allows us to achieve an optimal range of values spanned by the thinnest and thickest phantoms. These results facilitate the subtraction of tissue in the periphery of the breast, and aid in discriminating between contrast agent uptake in glandular tissue and subtraction artefacts.

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