X-ray phase contrast imaging of the breast: Analysis of tissue simulating materials^{a)}

Srinivasan Vedantham^{b)} and Andrew Karellas

Department of Radiology, University of Massachusetts Medical School, Worcester, Massachusetts 01655

(Received 3 January 2013; revised 7 February 2013; accepted for publication 21 February 2013; published 15 March 2013)

Purpose: Phase contrast imaging, particularly of the breast, is being actively investigated. The purpose of this work is to investigate the x-ray phase contrast properties of breast tissues and commonly used breast tissue substitutes or phantom materials with an aim of determining the phantom materials best representative of breast tissues.

Methods: Elemental compositions of breast tissues including adipose, fibroglandular, and skin were used to determine the refractive index, $n = 1 - \delta + i\beta$. The real part of the refractive index, specifically the refractive index decrement (δ), over the energy range of 5–50 keV were determined using XOP software (version 2.3, European Synchrotron Radiation Facility, France). Calcium oxalate and calcium hydroxyapatite were considered to represent the material compositions of microcalcifications *in vivo*. Nineteen tissue substitutes were considered as possible candidates to represent adipose tissue, fibroglandular tissue and skin, and four phantom materials were considered as possible candidates to represent microcalcifications. For each material, either the molecular formula, if available, or the elemental composition based on weight fraction, was used to determine δ . At each x-ray photon energy, the absolute percent difference in δ between the breast tissue and the substitute material was determined, from which three candidates were selected. From these candidate tissue substitutes, the material that minimized the absolute percent difference in linear attenuation coefficient μ , and hence β , was considered to be best representative of that breast tissue.

Results: Over the energy range of 5–50 keV, while the δ of CB3 and fibroglandular tissue-equivalent material were within 1% of that of fibroglandular tissue, the μ of fibroglandular tissue-equivalent material better approximated the fibroglandular tissue. While the δ of BR10 and adipose tissue-equivalent material were within 1% of that of adipose tissue, the tissue-equivalent material better approximated the adipose tissue in terms of μ . Polymethyl methacrylate, a commonly used tissue substitute, exhibited δ greater than fibroglandular tissue by $\sim 12\%$. The A-150 plastic closely approximated the skin. Several materials exhibited δ between that of adipose and fibroglandular tissue. However, there was an energy-dependent mismatch in terms of equivalent fibroglandular weight fraction between δ and μ for these materials. For microcalcifications, aluminum and calcium carbonate were observed to straddle the δ and μ of calcium oxalate and calcium hydroxyapatite. Aluminum oxide, commonly used to represent microcalcifications in the American College of Radiology recommended phantoms for accreditation exhibited δ greater than calcium hydroxyapatite by $\sim 23\%$.

Conclusions: A breast phantom comprising A-150 plastic to represent the skin, commercially available adipose and fibroglandular tissue-equivalent formulations to represent adipose and fibroglandular tissue, respectively, was found to be best suited for x-ray phase-sensitive imaging of the breast. Calcium carbonate or aluminum can be used to represent microcalcifications. © 2013 American Association of Physicists in Medicine. [<http://dx.doi.org/10.1118/1.4794503>]

Key words: phase contrast, interferometry, refraction, diffraction, mammography, phantom

I. INTRODUCTION

Since the early 1990s, various approaches^{1–12} for phase-sensitive x-ray imaging have been investigated. In addition, for a selected approach there are several choices for technological implementation. As an example, in Talbot interferometry, it is possible to determine the phase shift either from multiple images acquired by shifting the analyzer or phase grating with respect to each other,⁷ or, by tilting one grating with respect to the other by a small angle.^{13,14} Phase contrast imaging has attracted considerable attention for breast

imaging.^{8–11} To evaluate these choices for this application, it is essential to use a tissue substitute or phantom material that mimics the phase properties of the breast tissue. When x-rays propagate through an object, the associated phase and intensity changes can be represented by the object's complex index of refraction, $n = 1 - \delta + i\beta$, where δ is the refractive index decrement that is responsible for the phase shift, and β is the absorption index. In the above equation, the energy dependence of δ and β , and consequently n is implicit. At energy E and hence wavelength λ , β is related to the linear attenuation coefficient μ by $\mu = \frac{4\pi\beta}{\lambda}$, and is the basis for image

TABLE I. Substitute materials for breast tissues are ranked in order of their absolute difference in δ from the target breast tissue over the energy range of 5–50 keV. For each target breast tissue in column 1, the reference source for elemental composition is provided in column 2. For each substitute, the material, reference source for elemental composition or the molecular formula, mean $\pm$ standard deviation in $\% \delta_{\text{diff}}$ over the energy range, and the $\% \delta_{\text{diff}}$ range [minimum, maximum] are provided.

Tissue	Source	Substitute 1	Substitute 2	Substitute 3
Skin	Ref. 19	CB2	CB1	A-150
		Ref. 25	Ref. 25	Ref. 27
		0.61% $\pm$ 0.07% [0.34%, 0.65%]	0.94% $\pm$ 0.07% [0.67%, 0.99%]	3.54% $\pm$ 0.09% [3.14%, 3.59%]
Fibroglandular	Ref. 19	Fibroglandular-equivalent ^a	CB3	Water
			Ref. 25	H ₂ O
		−0.07% $\pm$ 0.07% [−0.39%, −0.03%]	−1.07% $\pm$ 0.07% [−1.37%, −1.02%]	−2.95% $\pm$ 0.02% [−2.96%, −2.88%]
	Ref. 24	CB3	Fibroglandular-equivalent ^a	Water
		Ref. 25		H ₂ O
		−0.28% $\pm$ 0.08% [−0.59%, −0.23%]	0.73% $\pm$ 0.07% [0.40%, 0.76%]	−2.18% $\pm$ 0.02% [−2.19%, −2.11%]
Adipose	Ref. 19	Adipose-equivalent ^a	BR10	Polypropylene
			Ref. 25	Ref. 29
		−0.19% $\pm$ 0.01% [−0.22%, −0.18%]	0.30% $\pm$ 0.01% [0.22%, 0.30%]	−0.56% $\pm$ 0.04% [−0.72%, −0.53%]
	Ref. 24	Adipose-equivalent ^a	BR10	Polypropylene
			Ref. 25	Ref. 29
		−0.13% $\pm$ 0.02% [−0.14%, −0.07%]	0.35% $\pm$ 0.02% [0.34%, 0.38%]	−0.50% $\pm$ 0.02% [−0.57%, −0.49%]
Microcalcifications	Calcium	Aluminum	Calcium carbonate	Aluminum oxide
	Oxalate	Al	CaCO ₃	Al ₂ O ₃
	Ref. 28	21.38% $\pm$ 0.57% [21.2%, 24.3%]	30.37% $\pm$ 0.14% [29.7%, 30.6%]	81.39% $\pm$ 0.6% [81.2%, 84.9%]
		Calcium carbonate	Aluminum	Aluminum oxide
	Calcium hydroxyapatite	CaCO ₃	Al	Al ₂ O ₃
	Ref. 28	−11.14% $\pm$ 0.08% [−11.4%, −11.1%]	−17.27% $\pm$ 0.39% [−17.4%, −15.0%]	23.63% $\pm$ 0.46% [23.3%, 26.4%]

^aElemental composition and density data for commercially available fibroglandular and adipose equivalent tissue substitutes were provided by the manufacturer (CIRS Inc., Norfolk, VA).

contrast in attenuation-based breast imaging techniques such as conventional mammography, digital breast tomosynthesis, and dedicated breast CT.

Spiers¹⁵ observed that the mass attenuation coefficient for any partial interaction process, such as the photoelectric interaction, was proportional to the product of electron density (ρ_e) and $Z^m - 1$, where Z is the atomic number and the value of the power m depended on the partial interaction process considered. The analysis by White¹⁶ indicated that the values for the power m for photon and electron interactions were energy-dependent and proposed a method^{17,18} that stressed the importance of considering the electron density and the effective atomic number in formulating tissue substitutes. Several tissue substitutes suitable for medical imaging in general, and for breast imaging in particular, have been formulated largely based on this method. The purpose of this report is to investigate if these tissue substitutes are also suitable for phase-sensitive x-ray imaging of the breast. Specifically, the difference in δ between the substitute materials and the target breast tissue were determined, and materials suitable for phase-sensitive x-ray imaging of the breast were identified. Once the substitute materials were identified, the choice of

material best representative for breast imaging was refined by considering the linear attenuation coefficient.

II. METHODS AND MATERIALS

II.A. Material composition data

In the absence of any abnormalities, the breast tissue can be broadly classified into comprising skin, fibroglandular and adipose tissues. Elemental composition of skin, fibroglandular and adipose tissues were provided by Hammerstein *et al.*¹⁹ In their report,¹⁹ the elements S, P, K, and Ca were grouped together as “ash.” We approximated “ash” as phosphorous for consistency with prior studies that used mass attenuation and mass energy absorption coefficients based on elemental composition.^{20–23} An updated report²⁴ on the elemental composition of fibroglandular and adipose tissues was also used to determine the refractive index decrement. Nineteen phantom materials were considered as substitutes for skin, fibroglandular and adipose tissues, including commonly used tissue substitutes such as polymethyl methacrylate (PMMA), BR10, BR12, paraffin wax, and solid water. Elemental

FIG. 1. Real part of the refractive index, specifically the refractive index decrement δ of breast tissues and substitute materials listed in Table I. For microcalcifications, calcium carbonate and aluminum were found to straddle the refractive index decrements of calcium oxalate and calcium hydroxyapatite in the energy range of 5–50 keV.

composition of epoxy resins such as BR10, BR12, CB1–CB4 were obtained from White *et al.*²⁵ and for solid water from Constantinou *et al.*²⁶ Elemental composition data for commercially available adipose and fibroglandular-equivalent material were provided by the manufacturer (CIRS Inc., Norfolk, VA). For all other tissue substitute materials, the elemental composition data were obtained from NIST databases.^{27–29} Microcalcifications can be broadly classified based on its composition either as an oxalate or as a phosphate. Calcium oxalate²⁸ ($\text{C}_2\text{H}_2\text{CaO}_5$) and calcium hydroxyapatite²⁸ [$\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$] were considered to represent microcalcifications *in vivo*. Four materials (Al, Au, Al_2O_3 , and CaCO_3) were considered as substitutes for microcalcifications. Among the materials considered as substitutes for microcalcifications, Au is used as signal objects in a contrast-detail phantom (CD-MAM 3.4, Artinis Medical Systems B.V., The Netherlands) designed for evaluating mammography,^{30,31} Al_2O_3 is used to represent microcalcifications in American College of Radiology (ACR) recommended phantoms for accreditation (e.g., Model 156, Gammex Inc., Middleton, WI), and CaCO_3 is used in mammography phantoms, typically for research (e.g., Model 012A, CIRS Inc., Norfolk, VA). For each tissue or substitute material, if the molecular formula was known, then the

molecular formula was used to determine δ . If the molecular formula was not known, then the elemental composition in terms of weight fraction was used to determine δ . For some substitute materials, if the sum of weight fractions of the constituent elements did not result in unity, then the weight fractions of all constituent elements were scaled so that their sum resulted in unity.

II.B. Determination of suitable substitute materials

Since the goal of this work was to identify tissue substitutes for phase-sensitive x-ray imaging of the breast, we prioritized selection of the tissue substitute candidate materials based on the refractive index decrement δ , followed by determination of their suitability based on μ , and hence β . At x-ray photon energy, E , the energy-dependent refractive index decrement of the breast tissue represented as $\delta_T(E)$ and that of the substitute material $\delta_S(E)$ were determined using the XOP software³² (Version 2.3, European Synchrotron Radiation Facility, France). X-ray photon energies from 5 to 50 keV, in steps of 1 keV, were considered as it is representative of the range used in several studies on phase contrast imaging.^{4–8,33}

FIG. 2. Linear attenuation coefficient μ that is related to the imaginary part of the refractive index β by $\mu = \frac{4\pi\beta}{\lambda}$, where λ is the wavelength corresponding to energy E is shown.

The percent difference in δ between the tissue and the substitute material was determined as per Eq. (1),

$$\% \delta_{\text{diff}}(E) = \frac{\delta_S(E) - \delta_T(E)}{\delta_T(E)} \times 100. \quad (1)$$

The substitute materials were ranked in increasing values of $|\% \delta_{\text{diff}}(E)|$, and three candidates tissue substitutes were determined. For each of these candidates and the target breast tissue, the linear attenuation coefficient μ was determined based on its mass density and the mass attenuation coefficient using XCOM database of NIST.³⁴ The NIST database was chosen as the values of β provided by XOP does not include coherent scatter.³² Among these candidates, the material that minimized the absolute percent difference in linear attenuation coefficient μ , and hence β , was considered to be the best representative of that breast tissue.

III. RESULTS AND DISCUSSION

Table I lists three choices for substitute materials ranked in order of $|\% \delta_{\text{diff}}(E)|$ for each tissue type and for

microcalcifications. For each substitute, the material name, reference source for elemental composition or the molecular formula, mean $\pm$ standard deviation in $\% \delta_{\text{diff}}$ over the energy range of 5–50 keV, and the range [minimum, maximum] of $\% \delta_{\text{diff}}$ within the energy range considered are provided. For the energy range of 5–50 keV considered, the ranked order of the three tissue substitutes shown in Table I did not change with x-ray photon energy. Figure 1 (log-log plot) shows the refractive index decrement of breast tissues and substitute materials listed in Table I plotted as a function of x-ray photon energy. For skin, fibroglandular and adipose tissues good visual agreement between the tissue and the substitute materials are observed. Aluminum and calcium carbonate were observed to straddle the refractive index decrements of calcium oxalate and calcium hydroxyapatite. The $\delta(E)$ of aluminum oxide (Al_2O_3) that is used to represent microcalcifications in ACR recommended phantom for accreditation was observed to be higher than calcium hydroxyapatite by $\sim 23\%$ over the energy range of 5–50 keV.

For the substitute materials identified in terms of δ in Table I, the linear attenuation coefficients as a function of

FIG. 3. Three tissue substitute materials exhibited δ and μ values between that of adipose and fibroglandular breast tissue over at least 50% of the energy range considered are shown. With the exception of BR10 over the narrow range or 30–35 keV, the equivalent fibroglandular fraction of δ and μ were substantially different.

energy is shown in Fig. 2 (log-log plot). For adipose and fibroglandular tissues, the linear attenuation coefficients were determined using elemental composition from Hammerstein *et al.*¹⁹ and Poletti *et al.*²⁴ and averaged. A-150 was best representative of skin. For fibroglandular tissue, either the commercially available tissue substitute or water can be a good choice. The commercially available tissue substitute was found to be best representative of adipose tissue. Aluminum and calcium carbonate were observed to straddle the linear attenuation coefficients of calcium oxalate and calcium hydroxyapatite.

Breast tissue substitutes with desired weight fraction of fibroglandular tissue, often referred to as glandular fraction (f_g), can be formulated as a weighted mixture of adipose and fibroglandular tissue substitutes. We investigated if some of the tissue substitute materials that exhibit $\delta(E)$ within the range bounded by adipose and fibroglandular tissues could be of use as phantom material. Seven tissue substitutes (CB3, water, solid water, paraffin wax, polyethylene, BR12, and BR10) were identified to exhibit $\delta(E)$ over the aforementioned range. Elemental composition and density data for breast tissue as a function of f_g tabulated by Boone²⁰ was used to determine $\delta(f_g, E)$. Regression analysis indicated a linear

dependence between $\delta(f_g, E)$ and f_g . Using the linear fit coefficients at each energy E , the equivalent fibroglandular weight fraction (f_g) for the seven substitute materials were determined (Table II). However, among these materials, only CB3, BR10, and BR12 were found to exhibit μ values within the range bounded by adipose and fibroglandular tissues. $\mu(f_g, E)$ as a function of f_g was determined from the mass attenuation coefficients and density using the mixture rule. Figure 3 shows that the equivalent fibroglandular weight fraction f_g for the three substitute materials in terms of δ and μ . In terms of δ , all three materials exhibited minimal variation in f_g over the range of x-ray photon energy considered. However, in terms of μ , substantial variation in f_g was observed with x-ray photon energy. With the exception of BR10 over the narrow range of 30–35 keV, the equivalent fibroglandular fraction of δ and μ were substantially different. Considering the large difference in f_g at a given energy between δ and μ for the three tissue substitutes, a mixture by weight of adipose and fibroglandular tissue-equivalent material to obtain a breast phantom with the desired f_g would be preferable.

TABLE II. Equivalent fibroglandular weight fraction (f_g) in terms of δ for seven tissue substitute materials that exhibited $\delta(E)$ between that of adipose and fibroglandular breast tissue over the energy range of 5–50 keV. For each tissue substitute material, the mean, the standard deviation, the minimum, and the maximum of f_g over 5–50 keV are provided.

Tissue substitute material	Equivalent fibroglandular weight fraction (f_g)			
	Mean	Standard deviation	Minimum	Maximum
CB3	0.91	0.01	0.88	0.94
Water	0.72	0.01	0.71	0.74
Solid water	0.58	0.01	0.56	0.60
Paraffin wax	0.31	0.01	0.29	0.33
Polyethylene	0.27	0.01	0.25	0.29
BR12	0.19	0.01	0.18	0.21
BR10	0.04	0.01	0.03	0.07

TABLE III. Percent difference in refractive index decrement computed with respect to fibroglandular tissue for materials that exhibited increased $\delta(E)$ over fibroglandular tissue in the energy range of 5–50 keV.

Tissue substitute material	% difference in δ with respect to fibroglandular tissue			
	Mean	Standard deviation	Minimum	Maximum
Polycarbonate	10.50	0.06	10.28	10.54
Polymethyl methacrylate (PMMA)	12.17	0.05	11.98	12.20
Polyethylene terephthalate (Mylar)	25.51	0.04	25.37	25.53
Polyvinyl chloride (PVC)	26.19	0.29	25.90	26.84
Teflon	84.67	0.18	84.57	85.38

FIG. 4. For the five materials that exhibited increased $\delta(E)$ over fibroglandular tissue, (a) the percent increase in $\delta(E)$, and (b) the percent difference in $\mu(E)$ with respect to fibroglandular tissue are shown. The percent difference in $\mu(E)$ with respect to fibroglandular tissue is energy-dependent.

Table III shows five materials that exhibited $\delta(E)$ greater than that of fibroglandular tissue.¹⁹ These materials provide a relatively wide range of $\sim 10\%$ – 85% increase in $\delta(E)$ over fibroglandular tissue [Fig. 4(a)] and can be potentially useful as signal objects. However, the percent difference in $\mu(E)$ with respect to fibroglandular tissue is energy-dependent [Fig. 4(b)].

For mammography dosimetry as well as phantom studies, the breast is typically approximated as a 50/50 mixture of adipose and fibroglandular tissue by weight fraction. Recent clinical studies^{35–37} using dedicated breast CT have shown that the average fibroglandular volume fraction to be

TABLE IV. δ -values ($\times 10^{-6}$) for breast tissues. For adipose and fibroglandular tissue, the average of δ -values obtained using elemental composition from Refs. 19 and 24 is shown.

Energy (keV)	Skin	Adipose	Fibroglandular	CaCO ₃
5	10.022	8.627	9.559	23.150
6	6.943	5.980	6.622	16.255
7	5.092	4.389	4.857	11.978
8	3.894	3.357	3.714	9.175
9	3.074	2.651	2.932	7.247
10	2.488	2.146	2.373	5.866
11	2.055	1.773	1.960	4.845
12	1.726	1.490	1.647	4.068
13	1.470	1.269	1.403	3.464
14	1.268	1.094	1.209	2.985
15	1.104	0.953	1.053	2.598
16	0.970	0.837	0.925	2.282
17	0.859	0.742	0.819	2.021
18	0.766	0.661	0.731	1.802
19	0.688	0.594	0.656	1.616
20	0.620	0.536	0.592	1.458
21	0.563	0.486	0.537	1.322
22	0.513	0.443	0.489	1.204
23	0.469	0.405	0.447	1.102
24	0.431	0.372	0.411	1.012
25	0.397	0.343	0.379	0.932
26	0.367	0.317	0.350	0.861
27	0.340	0.294	0.325	0.799
28	0.316	0.273	0.302	0.743
29	0.295	0.255	0.281	0.692
30	0.276	0.238	0.263	0.647
31	0.258	0.223	0.246	0.605
32	0.242	0.209	0.231	0.568
33	0.228	0.197	0.217	0.534
34	0.215	0.185	0.205	0.503
35	0.202	0.175	0.193	0.475
36	0.191	0.165	0.183	0.449
37	0.181	0.156	0.173	0.425
38	0.172	0.148	0.164	0.403
39	0.163	0.141	0.156	0.382
40	0.155	0.134	0.148	0.363
41	0.148	0.127	0.141	0.346
42	0.141	0.121	0.134	0.329
43	0.134	0.116	0.128	0.314
44	0.128	0.111	0.122	0.300
45	0.122	0.106	0.117	0.287
46	0.117	0.101	0.112	0.275
47	0.112	0.097	0.107	0.263
48	0.108	0.093	0.103	0.252
49	0.103	0.089	0.099	0.242
50	0.099	0.086	0.095	0.232

substantially lower. Transforming the fibroglandular volume fraction to weight fraction, the average f_g is $\sim 15\%$ – 20% . Additionally, studies^{38,39} using dedicated breast CT have shown that the breast skin thickness is ~ 1.45 mm. Hence, a breast phantom comprising ~ 1.45 mm shell of A-150 plastic to represent the skin and a weighted mixture of adipose and fibroglandular tissue-equivalent substitutes to provide fibroglandular weight fraction of $\sim 15\%$ – 20% would be best suited for

x-ray phase sensitive imaging. Such a phantom would also be well-suited for attenuation-based conventional mammography, digital breast tomosynthesis and dedicated breast CT. Either Al or CaCO_3 could be used to represent microcalcifications. Soft-tissue abnormalities can be represented either by fibroglandular tissue-equivalent material or by several of the materials considered in the study. However, it is important to note that while the percent difference in δ with respect to the background will be largely energy independent, the percent difference in μ with respect to the background will be energy dependent.

The δ values of breast tissues are provided in Table IV, and could be of assistance to researchers conducting numerical simulation studies of x-ray phase contrast imaging of the breast. We prioritized selection of the substitute material based on the refractive index decrement as many of these materials were formulated for x-ray attenuation imaging and have been analyzed in the past.²⁵ At x-ray photon energy E and hence wavelength λ , away from photoelectric absorption edges, the refractive index decrement (δ) is proportional to the electron density (ρ_e) and is related by^{40,41} $\delta = \frac{\rho_e r_0 \lambda^2}{2\pi}$, where r_0 is the classical electron radius. Hence, the observation that adipose and fibroglandular tissue-equivalent substitutes were better suited for phase contrast imaging is consistent with expectations as they were formulated with consideration for electron density.

IV. CONCLUSION

The commonly used substitute materials for attenuation-based conventional mammography such as adipose and fibroglandular tissue-equivalent formulations were also suitable for x-ray phase-sensitive imaging of the breast over the energy range of 5–50 keV. While several additional materials exhibited δ between that of adipose and fibroglandular tissue, there was an energy-dependent mismatch in terms of equivalent fibroglandular weight fraction between δ and μ for these materials, limiting their application. PMMA, a commonly used tissue substitute, was found to exhibit δ -values greater than fibroglandular tissue by $\sim 12\%$ and showed energy-dependent difference in μ with respect to fibroglandular tissue. Calcium carbonate and aluminum can serve as substitute materials for microcalcifications as their δ and μ values were found to straddle that of calcium oxalate and calcium hydroxyapatite over the energy range considered.

ACKNOWLEDGMENTS

This work was supported in part by National Institutes of Health (NIH) Grant No. R01 CA128906 and in part by R21 CA134128. The contents are solely the responsibility of the authors and do not represent the official views of the NIH or the NCI. The authors thank Moustafa Zerhouni, CIRS Inc., for providing the elemental composition and density data of their adipose and fibroglandular equivalent tissue substitutes.

- ^{a)}Some contents of this work were presented at the 54th Annual Meeting of the American Association of Physicists in Medicine, Charlotte, NC, July 2012.
- ^{b)}Author to whom correspondence should be addressed. Electronic mail: srinivasan.vedantham@umassmed.edu; Telephone: (508) 856-1241; Fax: (508) 856-6363.
- ¹T. J. Davis, D. Gao, T. E. Gureyev, A. W. Stevenson, and S. W. Wilkins, "Phase-contrast imaging of weakly absorbing materials using hard x-rays," *Nature (London)* **373**(6515), 595–598 (1995).
- ²A. Snigirev, I. Snigireva, V. Kohn, S. Kuznetsov, and I. Schelokov, "On the possibilities of x-ray phase contrast microimaging by coherent high-energy synchrotron radiation," *Rev. Sci. Instrum.* **66**(12), 5486–5492 (1995).
- ³A. Momose and J. Fukuda, "Phase-contrast radiographs of nonstained rat cerebellar specimen," *Med. Phys.* **22**(4), 375–379 (1995).
- ⁴X. Wu and H. Liu, "Clinical implementation of x-ray phase-contrast imaging: Theoretical foundations and design considerations," *Med. Phys.* **30**(8), 2169–2179 (2003).
- ⁵E. E. Bennett, R. Kopace, A. F. Stein, and H. Wen, "A grating-based single-shot x-ray phase contrast and diffraction method for in vivo imaging," *Med. Phys.* **37**(11), 6047–6054 (2010).
- ⁶D. Chapman, W. Thomlinson, R. E. Johnston, D. Washburn, E. Pisano, N. Gmur, Z. Zhong, R. Menk, F. Arfelli, and D. Sayers, "Diffraction enhanced x-ray imaging," *Phys. Med. Biol.* **42**(11), 2015–2025 (1997).
- ⁷F. Pfeiffer, T. Weitkamp, O. Bunk, and C. David, "Phase retrieval and differential phase-contrast imaging with low-brilliance x-ray sources," *Nat. Phys.* **2**(4), 258–261 (2006).
- ⁸M. Stampanoni, Z. Wang, T. Thuring, C. David, E. Roessl, M. Trippel, R. A. Kubik-Huch, G. Singer, M. K. Hohl, and N. Hauser, "The first analysis and clinical evaluation of native breast tissue using differential phase-contrast mammography," *Invest. Radiol.* **46**(12), 801–806 (2011).
- ⁹E. Castelli, M. Tonutti, F. Arfelli, R. Longo, E. Quaia, L. Rigon, D. Sanabor, F. Zanconati, D. Dreossi, A. Abrami, E. Quai, P. Bregant, K. Casarin, V. Chenda, R. H. Menk, T. Rokvic, A. Vascotto, G. Tromba, and M. A. Cova, "Mammography with synchrotron radiation: First clinical experience with phase-detection technique," *Radiology* **259**(3), 684–694 (2011).
- ¹⁰E. D. Pisano, R. E. Johnston, D. Chapman, J. Geradts, M. V. Iacocca, C. A. Livasy, D. B. Washburn, D. E. Sayers, Z. Zhong, M. Z. Kiss, and W. C. Thomlinson, "Human breast cancer specimens: Diffraction-enhanced imaging with histologic correlation—improved conspicuity of lesion detail compared with digital radiography," *Radiology* **214**(3), 895–901 (2000).
- ¹¹T. Tanaka, C. Honda, S. Matsuo, K. Noma, H. Oohara, N. Nitta, S. Ota, K. Tsuchiya, Y. Sakashita, A. Yamada, M. Yamasaki, A. Furukawa, M. Takahashi, and K. Murata, "The first trial of phase contrast imaging for digital full-field mammography using a practical molybdenum x-ray tube," *Invest. Radiol.* **40**(7), 385–396 (2005).
- ¹²A. Bravin, P. Coan, and P. Suortti, "X-ray phase-contrast imaging: From pre-clinical applications towards clinics," *Phys. Med. Biol.* **58**(1), R1–R35 (2013).
- ¹³H. Itoh, K. Nagai, G. Sato, K. Yamaguchi, T. Nakamura, T. Kondoh, C. Ouchi, T. Teshima, Y. Setomoto, and T. Den, "Two-dimensional grating-based x-ray phase-contrast imaging using Fourier transform phase retrieval," *Opt. Express* **19**(4), 3339–3346 (2011).
- ¹⁴N. Bevins, J. Zambelli, K. Li, Z. Qi, and G. H. Chen, "Multicontrast x-ray computed tomography imaging using Talbot-Lau interferometry without phase stepping," *Med. Phys.* **39**(1), 424–428 (2012).
- ¹⁵F. W. Spiers, "Effective atomic number and energy absorption in tissues," *Br. J. Radiol.* **19**, 52–63 (1946).
- ¹⁶D. R. White, "An analysis of the z-dependence of photon and electron interactions," *Phys. Med. Biol.* **22**(2), 219–228 (1977).
- ¹⁷D. R. White, "The formulation of tissue substitute materials using basic interaction data," *Phys. Med. Biol.* **22**(5), 889–899 (1977).
- ¹⁸D. R. White, "Effective atomic numbers in the formulation of tissue substitute materials for photons," *Radiat. Res.* **76**, 23–31 (1978).
- ¹⁹G. R. Hammerstein, D. W. Miller, D. R. White, M. E. Masterson, H. Q. Woodard, and J. S. Laughlin, "Absorbed radiation dose in mammography," *Radiology* **130**(2), 485–491 (1979).
- ²⁰J. M. Boone, "Glandular breast dose for monoenergetic and high-energy x-ray beams: Monte Carlo assessment," *Radiology* **213**(1), 23–37 (1999).
- ²¹S. Vedantham, L. Shi, A. Karellas, and F. Noo, "Dedicated breast CT: Radiation dose for circle-plus-line trajectory," *Med. Phys.* **39**(3), 1530–1541 (2012).

- ²²S. Vedantham, L. Shi, S. J. Glick, and A. Karellas, "Scaling-law for the energy dependence of anatomic power spectrum in dedicated breast CT," *Med. Phys.* **40**(1), 011901 (8pp.) (2013).
- ²³I. Sechopoulos, S. Vedantham, S. Suryanarayanan, C. J. D'Orsi, and A. Karellas, "Monte Carlo and phantom study of the radiation dose to the body from dedicated CT of the breast," *Radiology* **247**(1), 98–105 (2008).
- ²⁴M. E. Poletti, O. D. Goncalves, and I. Mazzaro, "X-ray scattering from human breast tissues and breast-equivalent materials," *Phys. Med. Biol.* **47**(1), 47–63 (2002).
- ²⁵D. R. White, R. J. Martin, and R. Darlison, "Epoxy resin based tissue substitutes," *Br. J. Radiol.* **50**(599), 814–821 (1977).
- ²⁶C. Constantinou, F. H. Attix, and B. R. Paliwal, "A solid water phantom material for radiotherapy x-ray and gamma-ray beam calibrations," *Med. Phys.* **9**(3), 436–441 (1982).
- ²⁷J. H. Hubbell and S. M. Seltzer, Tables of X-Ray Mass Attenuation Coefficients and Mass Energy-Absorption Coefficients (Version 1.4), National Institute of Standards and Technology, Gaithersburg, MD, 2004 (available URL: <http://physics.nist.gov/xaamdi>).
- ²⁸NIST, NIST Chemistry WebBook –NIST Standard Reference Database Number 69, National Institutes of Standards and Technology, Gaithersburg, MD, 2012 (available URL: <http://webbook.nist.gov/chemistry/>).
- ²⁹M. J. Berger, J. S. Coursey, M. A. Zucker, and J. Chang, ESTAR, PSTAR, and ASTAR: Computer Programs for Calculating Stopping-Power and Range Tables for Electrons, Protons, and Helium Ions (version 1.2.3), National Institutes of Standards and Technology, Gaithersburg, MD, 2005 (available URL: <http://www.nist.gov/pml/data/star/index.cfm>).
- ³⁰S. Suryanarayanan, A. Karellas, S. Vedantham, H. Ved, S. P. Baker, and C. J. D'Orsi, "Flat-panel digital mammography system: Contrast-detail comparison between screen-film radiographs and hard-copy images," *Radiology* **225**(3), 801–807 (2002).
- ³¹S. Suryanarayanan, A. Karellas, S. Vedantham, S. M. Waldrop, and C. J. D'Orsi, "A perceptual evaluation of JPEG 2000 image compression for digital mammography: Contrast-detail characteristics," *J. Digit Imaging* **17**(1), 64–70 (2004).
- ³²M. S. del Rio and R. J. Dejus, European Synchrotron Radiation Facility (ESRF), France, X-ray Oriented Programs (XOP), Version 2.3, Grenoble, France, 2009.
- ³³E. Fredenberg, M. Danielsson, J. W. Stayman, J. H. Siewerdsen, and M. Aslund, "Ideal-observer detectability in photon-counting differential phase-contrast imaging using a linear-systems approach," *Med. Phys.* **39**(9), 5317–5335 (2012).
- ³⁴M. J. Berger, J. H. Hubbell, S. M. Seltzer, J. Chang, J. S. Coursey, R. Sukumar, D. S. Zucker, and K. Olsen, XCOM: Photon Cross Sections Database, NIST Standard Reference Database 8 (XGAM), The National Institute of Standards and Technology (NIST), Gaithersburg, MD, 2011 (available URL: <http://www.nist.gov/pml/data/xcom/index.cfm>).
- ³⁵T. R. Nelson, L. I. Cervino, J. M. Boone, and K. K. Lindfors, "Classification of breast computed tomography data," *Med. Phys.* **35**(3), 1078–1086 (2008).
- ³⁶M. J. Yaffe, J. M. Boone, N. Packard, O. Alonzo-Proulx, S. Y. Huang, C. L. Peressotti, A. Al-Mayah, and K. Brock, "The myth of the 50-50 breast," *Med. Phys.* **36**(12), 5437–5443 (2009).
- ³⁷S. Vedantham, L. Shi, A. Karellas, and A. M. O'Connell, "Dedicated breast CT: Fibroglandular volume measurements in a diagnostic population," *Med. Phys.* **39**(12), 7317–7328 (2012).
- ³⁸S. Y. Huang, J. M. Boone, K. Yang, A. L. Kwan, and N. J. Packard, "The effect of skin thickness determined using breast CT on mammographic dosimetry," *Med. Phys.* **35**(4), 1199–1206 (2008).
- ³⁹L. Shi, S. Vedantham, A. Karellas, and A. M. O'Connell, "Skin thickness measurements using high-resolution flat-panel cone-beam dedicated breast CT," *Med. Phys.* **40**(3), 031913 (6pp.) (2013).
- ⁴⁰M. Bech, T. H. Jensen, R. Feidenhans'l, O. Bunk, C. David, and F. Pfeiffer, "Soft-tissue phase-contrast tomography with an x-ray tube source," *Phys. Med. Biol.* **54**(9), 2747–2753 (2009).
- ⁴¹Z. Qi, J. Zambelli, N. Bevins, and G. H. Chen, "Quantitative imaging of electron density and effective atomic number using phase contrast CT," *Phys. Med. Biol.* **55**(9), 2669–2677 (2010).