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Soft tissue small avascular tumor imaging with x-ray phase-contrast micro-CT in-line holography

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Abstract

To assess the feasibility of small soft tissue avascular tumor micro-CT imaging with x-ray phase-contrast in-line holography, we have studied micro-CT imaging with in-line geometry of small spheroidal avascular tumor models with quiescent cell core ($< 250 \mu\text{m}$) and various distributions of the proliferating cell density (PCD) forming the outer shell. We have simulated imaging with an ultrafast laser-based x-ray source with a Mo target. We observe phase-contrast enhancement of the tumor boundaries in the reconstructed transaxial images, resulting in improved detection of small soft tissue tumors, providing that the PCD density gradient is sufficiently large.

Keywords

micro-CT imaging; x-ray phase-contrast in in-line holography; soft tissue avascular tumor model; tumor detection

1. INTRODUCTION

One of the major drawbacks of CT and micro-CT is their rather poor density resolution (smallest density variation in the object that can be resolved in the image). In-line x-ray phase-contrast imaging is a promising new technology that might afford improved soft tissue resolution [1-11]. This imaging method requires an x-ray source with a sufficiently small effective focal spot size, suitable spectral distribution, and an appropriate imaging geometry. An ultrafast-laser-based x-ray (ULX) source fulfills these requirements [12]. Therefore, we have investigated micro-tomographic imaging of soft-tissue small avascular tumors with ULX under Fresnel conditions, because they are most suitable for laboratory *in vivo* imaging [1].

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2. MATERIALS AND METHODS

Using in-line geometry, we studied x-ray phase-contrast micro-CT imaging of small spheroidal avascular tumor models proposed by Jiang et al. [13] and Stein et al. [14]. We considered an invading tumor in an early stage of development (i.e. not containing a necrotic core) with quiescent cell core radius of 250 μm and diverse distributions of the proliferating cells forming the outer shell. This layer was modeled by various degrees of Gaussian blurring of the density profile across the interface with the surrounding tissue (FWHM in the 8–100 μm range). We used a simplified model of a mouse, namely a cylinder 28 mm in diameter and 300 mm in length. We assumed that the tumor was centrally located, that the tumor core had the same radiological properties as soft tissue, and that it was embedded in adipose tissue. Simulations were performed using an analytical model describing propagation of an x-ray wave through an object assuming that the “projection approximation” was valid, so that the amplitude $E_{out}(x,y)$ of the wave transmitted through the object was related to the amplitude $E_{in}(x,y)$ of the wave incident on the object as follows: $E_{out}(x,y) = \exp[i\phi(x,y) - a(x,y)] E_{in}(x,y)$, where $\phi(x,y)$ and $a(x,y)$ are the phase and the attenuation induced by the object, respectively. The free-space propagation from the object plane to the detector was modeled using a rigorous wave-optics formalism [15-18]. The following parameters of the imaging system were used in our simulations: $\sigma_S = \sigma_D = 0$ (point source and perfect detector), $M = 1.1$ and $M = M_{opt} = 2$ (optimum magnification corresponding to the point source and perfect detector), $R = 2$ m (total source-to-detector distance), and 20 keV x-ray energy. We created sets of micro-CT projection images and reconstructed them using a modified Feldkamp algorithm (Figs. 1-6). The data for Figs. 1 and 2 were created from 360 projection images, and, for Figs. 3-6, 1,440 projections were used. We also estimated image contrast in projection images for tumor models with diameter in the 0.2–2 mm range (Figs. 7, 8).

3. RESULTS AND DISCUSSION

We have observed phase-contrast enhancement of the image contrast at the boundaries of the tumor in the projection images, and even stronger enhancement in the reconstructed transaxial images. The boundary enhancement depends strongly on the electron density gradient in the proliferating cell region. It is very strong for FWHM = 8 μm , moderate at FWHM = 50 μm , and difficult to detect for FWHM = 100 μm . At large values of the tumor radius, absorption contrast dominates (Fig. 7) and contrast is almost independent of the gradient of electron density at the boundary. For small tumors ($r < 1$ mm), phase contrast dominates, but it rapidly decreases with increased blurring of the interface between the tumor and normal tissue.

4. CONCLUSIONS

X-ray phase-contrast micro-CT using in-line holography geometry could offer improved detection of small soft tissue avascular tumors in early stages of invasion, provided that the proliferating cell density gradient is sufficiently large.

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REFERENCES

1. Wilkins SW, Gureyev TE, Gao D, Pogany A, Stevenson AW. Phase-contrast imaging using polychromatic hard x-rays. *Nature*. 1996; 384:335–338.
2. Pogany A, Gao D, Wilkins SW. Contrast and resolution in imaging with a microfocus x-ray source. *Rev. Sci. Instr.* 1997; 68:2774–2782.
3. Gureyev TE, Raven C, Snigirev AA, Snigireva I, Wilkins SW. Hard x-ray quantitative noninterferometric phase-contrast imaging. *SPIE Proceedings*. 1999; 3659:356–364.
4. Gureyev TE, Stevenson AW, Paganin D, Mayo SC, Pogany A, Gao D, Wilkins SW. Quantitative methods in phase-contrast x-ray imaging. *J.Dig.Imag.* 2000; 13:121–126.
5. Gureyev TE, Stevenson AW, Paganin DM, Weitkamp T, Snigirev A, Snigireva I, Wilkins SW. Quantitative analysis of two-component samples using in-line hard x-ray images. *J. Synch. Rad.* 2002; 9:148–153.
6. Gureyev TE, Wilkins SW. On x-ray phase imaging with a point source. *J. Opt. Soc. Am.* 1998; A15:579–585.
7. Gureyev TE, Wilkins SW. On x-ray phase retrieval from polychromatic images. *Opt. Comm.* 1998; 147:229–232. 154, 391. (erratum).
8. Honda C, Ohara H, Ishisaka A, Shimada F, Endo T. X-ray Phase Imaging Using a X-ray Tube with a Small Focal Spot-Improvement of Image Quality in Mammography. *Jpn. J. Med. Phys.* 2002; 22:21–29.
9. Donnelly EF, Price RR, Pickens DR. Quantification of the effect of system and object parameters on edge enhancement in phase-contrast radiography. *Med. Phys.* 2003; 30:2888–2896. [PubMed: 14655935]
10. Wu X, Liu H. An experimental method of determining relative phase-contrast factor for x-ray imaging system. *Med. Phys.* 2004; 31(5):997–1002. [PubMed: 15191283]
11. Krol A, Kincaid RE Jr, Servol M, Kieffer J-C, Nesterets Y, Gureyev T, Stevenson A, Wilkins S, Ye H, Lipson E, Toth R, Pogany A, Coman I. Initial experimentation with in-line holography x-ray phase-contrast imaging with an ultrafast laser-based x-ray source. *Proceedings of the SPIE*. 2007; 6510:65100L.
12. Toth R, Kieffer JC, Fourmaux S, Ozaki T, Kincaid RE Jr, Krol A. Evaluation of ultrafast laser-based hard x-ray sources for phase-contrast imaging. *Physics of Plasmas*. 2007; 14:053506.
13. Jiang, Yi; Pjesivac-Grbovic, Jelena; Cantrell, Charles; Freyer, James P. A Multiscale Model for Avascular Tumor Growth. *Biophysical Journal*. Dec.2005 89:3884–3894. [PubMed: 16199495]
14. Stein, Andrew M.; Demuth, Tim; Mobley, David; Berens, Michael; Sander, Leonard M. A Mathematical Model of Glioblastoma Tumor Spheroid Invasion in a Three-Dimensional In Vitro Experiment. *Biophysical Journal*. Jan.2007 92:356–365. [PubMed: 17040992]
15. Nesterets YI, Wilkins SW, Gureyev TE, Pogany A, Stevenson AW. On the optimization of experimental parameters for x-ray in- phase-contrast imaging. *Rev. Sci. Instr.* 2005; 76:093706.
16. Born, M.; Wolf, E. *Principles of Optics*. 6th ed.. Pergamon, Oxford: 1980.
17. Cowley, JM. *Diffraction Physics*. 3rd ed.. North Holland, Amsterdam: 1995.
18. Barrett, H.; Swindell, W. *Radiological Imaging*. Rev. ed.. Academic Press; San Diego: 1981.

Fig. 1.

Top row: (left to right) tumor model with Gaussian boundary blurring $\text{FWHM} = 8 \mu\text{m}$, projection image ($M=2$), transaxial slice through the center obtained using tomographic reconstruction (modified Feldkamp) from 1,440 projections, and edges detected in the reconstructed image. Bottom row: (left to right) horizontal one-channel line profiles through the center of images for the object, projection, reconstruction, and edges. All images are normalized by their maxima.

Fig. 2.

Top row: (left to right) tumor model with Gaussian boundary blurring $\text{FWHM} = 8 \mu\text{m}$, projection image ($M = 1.1$), transaxial slice through the center obtained using tomographic reconstruction (modified Feldkamp) from 1,440 projections, and edges detected in the reconstructed image. Bottom row: (left to right) horizontal one-channel line profiles through the center of images for the object, projection, reconstruction, and edges. All images are normalized to their maxima.

Fig. 3.

Top row: (left to right) tumor model with Gaussian boundary blurring $\text{FWHM} = 20 \mu\text{m}$, projection image ($M = 2$), transaxial slice through the center obtained using tomographic reconstruction (modified Feldkamp) from 1440 projections, and edges detected in the reconstructed image. Bottom row: (left to right) horizontal one-channel line profiles through the center of images for the object, projection, reconstruction, and edges. All images are normalized to their maxima.

Fig. 4.

Top row: (left to right) tumor model with Gaussian boundary blurring $\text{FWHM} = 20 \mu\text{m}$, projection image ($M=1.1$), transaxial slice through the center obtained using tomographic reconstruction (modified Feldkamp) from 1,440 projections, and edges detected in the reconstructed image. Bottom row: (left to right) horizontal one-channel line profiles through the center of images for the object, projection, reconstruction, and edges. All images are normalized to their maxima.

Fig. 5.

Top row: (left to right) tumor model with Gaussian boundary blurring $\text{FWHM} = 50 \mu\text{m}$, projection image ($M=2$), transaxial slice through the center obtained using tomographic reconstruction (modified Feldkamp) from 360 projections, and edges detected in the reconstructed image. Bottom row: (left to right) horizontal one-channel line profiles through the center of images for the object, projection, reconstruction, and edges. All images are normalized to their maxima.

Fig. 6.

Top row: (left to right) tumor model with Gaussian boundary blurring $\text{FWHM} = 100 \mu\text{m}$, projection image ($M = 2$), transaxial slice through the center obtained using tomographic reconstruction (modified Feldkamp) from 360 projections, and edges detected in the reconstructed image. Bottom row: (left to right) horizontal one-channel line profiles through the center of images for the object, projection, reconstruction, and edges. All images are normalized to their maxima.

Fig. 7. Contrast vs. simulated tumor diameter d for 10, 50, and 100 μm (FWHM) proliferating-cell interface.

Fig. 8. Contrast vs. gaussian blurring [μm] (FWHM) of proliferating-cell interface, for 1 mm diameter simulated tumor. Contrast is defined as $(\text{Max} - \text{Min}) / (\text{Max} + \text{Min})$