Towards Clinical X-Ray Phase-Contrast CT

Demonstration of Enhanced Soft-Tissue Contrast in Human Specimen

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SUPPLEMENTAL METHODS

In the following, we give a concise summary of the PCCT technique and its physical fundamentals, based on previous publications. The description of the physical basics of attenuation imaging is oriented at the textbook by Barrett and Swindell [barrett1981].

Attenuation and phase (refraction) projection. The transmitted x-ray intensity behind an object is given by

(1) $I = I_0 e^{-\int ds\, \mu(x,y,z)}$,

where I_0 is the intensity of the incident beam, $\mu(x,y,z)$ is the linear attenuation coefficient for x rays inside the object, and the integral over coordinate s is along the propagation direction of the x-ray beam. (Compare Fig. 1a in the article.) In conventional CT, we measure I and I_0, from which the projection of the linear attenuation coefficient given by

(2) $p = -\ln \frac{I}{I_0} = \int ds\, \mu(x,y,z)$

is calculated.

The refraction angle α of x-rays, additionally measured in differential phase-contrast CT methods, and so in PCCT, is essentially given by

$$(3)\quad \alpha = \frac{\partial}{\partial t}\int ds\,\delta(x,y,z),$$

where $\delta(x,y,z)$ is the local deviation of the real part of the complex refractive index (compare below) from unity. The integration in Equation (3) is performed along coordinate *s*, i.e., along the x-ray propagation direction, just like for the attenuation projection in Equations (1) and (2). The directional derivative is taken along the *t*-direction perpendicular to the grating structures (see Fig. 1b). Thus, the refraction angle in the plane spanned by x-ray propagation direction and *t*-axis is measured. In all above equations, we have assumed that the deviation from the straight ray due to the minute beam deflection is negligible and causes no image blur.

Both μ and δ depend on the x-ray wavelength (compare below). Hence, to incorporate the effect of an x-ray spectrum, the measured intensity in (1) must be weighted with the spectral distribution function and integrated over all wavelengths. Similarly, the deflection angle in (3) needs to be weighted with the spectral intensity distribution that contributes to the phase signal. Due to the x-ray-energy dependent efficiency of the Talbot interferometer [engelhardt2008], the phase measurement corresponds to an effective x-ray energy spectrum that differs from that of the simultaneously conducted conventional attenuation measurement (compare [herzen2009]). A broad x-ray spectrum can introduce beam-hardening artifacts in the attenuation reconstruction, and can also influence the phase reconstruction. Although, we found that the artifacts are much less pronounced for the phase images (compare article).

The projections acquired in our measurement are two-dimensional images of the form $p_\theta(t,z)$ and $\alpha_\theta(t,z)$, recorded for projection angles θ, where the sample rotates around the *z* axis (Fig. 1b). Using tomographic reconstruction algorithms (see Methods

in the article), we recover the linear attenuation coefficient $\mu(x,y,z)$ from $p_\theta(t,z)$ and the refractive index decrement $\delta(x,y,z)$ from $\alpha_\theta(t,z)$, where the *xyz* coordinate system is the sample coordinate system, rotated around the *z* axis by the angle θ.

Projections from interferometer phase scans. To measure the projection images $p_\theta(t,z)$ and $\alpha_\theta(t,z)$ with the grating interferometer, we apply a Moiré phase-stepping technique [creath1988,weitkamp2005]. Translation of one of the interferometer gratings, in a direction perpendicular to the grating structure, causes an intensity oscillation in the Moiré pattern measured by the detector. To a first order approximation, we may assume the intensity oscillation recorded in each pixel to be of the form, $I_j = \hat{I} + I_1 \cos(2\pi j/N + \varphi)$. Where j is an integer phase-step index running from 1 to N for a measurement, with N phase steps over one period. Calculating the discrete Fourier transform (DFT) of the recorded phase-stepping scan for each pixel provides the Fourier coefficients a_j, with $j = 0, ..., N-1$. The mean oscillation intensity is simply given by $\hat{I} = a_0$ and the oscillation amplitude is $I_1 = 2|a_1|$, where the factor 2 accounts for the corresponding negative frequency element ($j = N-1$) of the DFT. The phase shift is obtained as $\varphi = \text{atan2}(a_1)$, where atan2() is the function that returns the phase of the complex number a_1, with values in the range from $-\pi$ to $+\pi$.

To calculate the projections, a reference phase-stepping scan without the object in the beam path is recorded. In analogy to the above, $\hat{I}_r$, $I_{1,r}$, and φ_r are determined for the reference scan. The attenuation projections are then calculated as $p = -\ln(\hat{I}/\hat{I}_r)$ and the refraction angles (differential phase-contrast projections) as $\alpha = \Delta\varphi/(2\pi S)$. Here, we introduced the angular sensitivity $S = d/p_2$ of the grating interferometer [donath2009], where p_2 is the period of Grating G2, d is the distance between gratings G1 and G2, and the difference of angles $\Delta\varphi = \varphi - \varphi_r$ is measured modulo 2π in the range from $-\pi$ to $+\pi$. We have neglected the small decrease in sensitivity caused by the additional distance of the sample from the G1 grating (compare [engelhardt2007] and [donath2009]).

The phase signal is contained only in the oscillating fraction of the recorded phase-stepping scan, which should be as high as possible. As a measure of quality for the interferometric phase images, we define the visibility $V = I_1/\hat{I}$, which gives the fraction of intensity that contributes to the intensity oscillation in the phase-stepping scan. The visibility will generally depend on the quality of the interferometer gratings being used, the geometry of the interferometer setup, and the x-ray spectrum.

Complex refractive index. The complex refractive index $n = 1 - \delta + i\beta$ can be used to describe attenuation and phase shift caused by a sample. The complex refractive index is a convenient number for the calculation of the propagation of wave fields. The complex amplitude U of an attenuated plane wave of wavelength λ, propagating along direction x, in a homogeneous medium with complex refractive index $n = 1 - \delta + i\beta$, can be described as $U = A_0 \exp[in(2\pi/\lambda)x)] = A_0 \exp[(2\pi/\lambda)x] \exp[-i\delta(2\pi/\lambda)x] \exp[-\beta(2\pi/\lambda)x]$.

The refractive index decrement δ of the homogeneous sample of thickness d thus causes a phase shift $\Phi = -\delta(2\pi/\lambda)d$ on the x-ray wave. In the general case of an inhomogeneous sample with refractive index distribution $\delta(x,y,z)$, the phase shift becomes $\Phi = -\frac{2\pi}{\lambda}\int ds\,\delta(x,y,z)$.

The intensity of the plane wave field $|U|^2 = |A_0|^2 \exp[-2\beta(2\pi/\lambda)x]$ decays with attenuation coefficient $\mu = 2\beta(2\pi/\lambda)$ along x. Note that μ, and not β, is obtained from the measurement. Conversion of measured μ values into β values requires knowledge of the x-ray wavelength λ, which, in most measurements and especially in measurements with a broad x-ray spectrum, is not well defined. Conversion should thus be avoided. Consequently, we keep and present our results in form of the measured pairs of δ and μ (rescaled to HU-P and HU numbers).

Refractive index decrement and linear attenuation coefficient. The *refractive index decrement* δ is related to the wavelength and the electron density inside the sample. For a mixture containing M types of atoms it can be expressed as

$$\delta = \frac{r_e \lambda^2}{2\pi} \sum_{i=1}^{M} N_i f_i^1 \approx \frac{r_e \lambda^2}{2\pi} \rho_e ,$$

for given x-ray wavelength λ, classical electron radius $r_e = 2.82 \cdot 10^{-15}$m, the atomic density N_i in atoms per unit volume for type i atoms, and the real part of the atomic scattering factor f_i^1 in the forward direction. The approximation on the right is valid, if the photon energy ($E \propto \lambda^{-1}$) of the incident x-ray radiation lies considerably above the binding energy of the contributing elemental absorption edges (compare [james1962: Chapter IV, 2(a)]). In this case, we may put $f_i^1 \approx Z_i$, where Z_i is the total number of electrons of a type i atom and the sum over elements in the above equation becomes approximately equal to the electron density ρ_e inside the sample. The refractive index decrement δ of a homogeneous sample of thickness d thus causes a phase shift $\Phi = \delta(2\pi/\lambda)d \approx r_e \lambda \rho_e d$, which is proportional to the electron density and the x-ray wavelength. For biological samples and clinically relevant x-ray energies, the x-ray energy is significantly above the absorption edges and, so, the phase signal is proportional to the electron density; $\alpha \propto \delta \propto \rho_e$.

The *linear attenuation coefficient* μ for a substance depends on the photon energy, the elemental composition of the substance, and its mass density. In the relevant photon energy range, μ is dominated by the photoelectric absorption μ_{PE} and Compton scattering μ_C terms [barrett1981], with $\mu \approx \mu_{PE} + \mu_C$. As a rule of thumb, we have that $\mu_{PE} \propto Z^4 E^{-3}$, where Z is the atomic number of the material [barrett1981].

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