The case for single-exposure angiography using energy-resolving photon-counting detectors: A theoretical comparison of signal and noise with conventional subtraction angiography

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ABSTRACT

Purpose: The use of energy-resolving photon-counting (EPC) x-ray detectors creates an opportunity for material specific x-ray imaging. An exciting potential application of this technique is energy-resolved angiography (ERA) in which the injected-iodine signal is determined from an analysis of x-ray energies in a single exposure rather than the subtraction of a mask image from a post-contrast-injection image, as used in conventional digital subtraction angiography (DSA). The purpose of this study is to explore the possibility of single-exposure angiography using EPC detectors by theoretically calculating the signal-difference-to-noise ratio (SDNR) per root entrance exposure (X) in an iodine-specific image that could be determined using spectral methods, and to compare this with the corresponding SDNR using DSA for the same x-ray exposure.

Methods: We model DSA by subtracting x-ray transmission measurements acquired using ideal energy-integrating x-ray detectors pre and post-injection of an iodine contrast agent. DSA image noise is calculated by propagating random fluctuations in the transmission measurements through the subtracted image. We model ERA by acquiring a single post-injection transmission measurement acquired using an ideal EPC x-ray detector operated with three energy bins. We then use a maximum likelihood parameter estimation technique to extract the iodine signal and theoretically calculate image noise using the Cramer Rao lower bound.

Results: Angiography using ideal EPC x-ray detectors can separate iodine-filled cavities of variable concentrations from a water-only background in a single x-ray exposure. For high iodine concentrations, the best SDNR/√X for DSA is approximately 1.5 times the best SDNR/√X for ERA and at low concentrations this factor reduces to 1.3. This difference of approximately 1.3 to 1.5 times is surprisingly small. While DSA in general provides better image quality for the same x-ray exposure, DSA has been unsuccessful in coronary applications because of motion-related image artifacts. Patient motion would, however, not be a problem when using ERA because only a single scan is required.

Conclusions: X-ray imaging using ideal energy-resolving photon-counting detectors has the potential to provide DSA-like angiographic images of iodinated vasculature in a single x-ray exposure, therefore eliminating motion-related image artifacts that limit the use of DSA in cardiac applications. ERA may potentially be used in for background removal in situations where DSA cannot be used, such as in cardiac imaging.

1. INTRODUCTION

Angiography using intra-arterial injections of an iodinated contrast agent is currently the reference standard for diagnosing coronary artery disease (CAD).\textsuperscript{1,2} Digital subtraction angiography (DSA), performed by subtracting pre and post-injection images, was developed to enhance visualization of the arterial lumen by removing overlying patient structures from the image and use smaller contrast injections and has been exceptionally successful for imaging near-stationary structures including the neural vasculature and extremities.\textsuperscript{3,4} However, the need for pre and post-injection exposures results in motion-related image artifacts in cardiac applications and DSA has been far less successful in diagnosing CAD. Image registration techniques have been developed in an attempt to retrospectively compensate for patient motion\textsuperscript{5-7} but have seen limited implementation in coronary applications.
The prospect of energy-resolving single-photon counting (EPC) detectors for x-ray image acquisition has identified a number of benefits over the usual approach in which the detector signal is proportional to total energy deposited by the spectrum of photons interacting during an image-acquisition interval. One exciting aspect is the potential for energy-resolved x-ray imaging where the energy of each interacting x-ray photon is estimated with the goal of determining the spectrum of interacting photons for each image pixel. It is anticipated that this information can be used to estimate the area density (g cm$^{-2}$) of various materials along the x-ray path for each pixel$^{8,9}$ This raises the potential for new advanced material-specific imaging such as angiography without requiring subtraction of a mask image from a post-contrast-injection image as used in DSA.$^{9,10}$ This would eliminate motion artifacts due to imperfect anatomic registration (important for cardiac angiography) and may enable new dynamic-contrast studies.

Many technical barriers must be overcome before EPC detectors can be used in diagnostic radiology applications. In particular, they must be able to operate at very high count rates that cannot be achieved at present. Also, when an x-ray photon interacts in the detector, it may deposit energy in more than one detector element. It will then be necessary to account for this by summing signals from near-by elements to get an estimate of total energy deposited$^{11,12}$ and prevent double counting which would result in increased image noise and noise correlations between elements.$^{13-15}$ This technique has recently been implemented in the Medipix-3 prototype.$^{16}$ In addition, the spectrum will be degraded by the random escape of characteristic and scattered photons$^{17}$ which subsequently impairs the ability to spectroscopically isolate materials.$^{18-20}$

Many researchers have identified a number of potential benefits of EPC detectors for use in mammographic and CT applications.$^{9,10,21}$ We explore the possibility of single-exposure angiography using EPC detectors by theoretically calculating the signal-difference-to-noise ratio (SDNR) in an iodine-specific image that could be determined using spectral methods, and comparing this with the corresponding SDNR using conventional subtraction angiography for the same x-ray exposure. This article is not a demonstration of what can be achieved at present, but provides an optimistic view of what could be achieved with EPC detectors.

2. THEORY

We consider the task of determining the iodine signal in a background of soft tissue. The iodine signal, $A_I$, is an estimate of the area density (g cm$^{-2}$) of iodine in each pixel with a statistical uncertainty $\sigma_I$. We let $A^b_i$ represent the iodine signal in a pixel where there is no iodine present (i.e. the background signal) and $\sigma_b$ be the corresponding statistical uncertainty. The signal-difference-to-noise ratio is then given by

$$\text{SDNR} = \frac{|A_I - A^b_i|}{\sqrt{\sigma_I^2 + \sigma_b^2}}$$

In the following subsections we briefly describe the measurement process for both DSA and ERA and how we calculate iodine image signal and noise. In all cases our measurement model assumes ideal energy resolution and unity quantum efficiency. All sources of noise apart from Poisson quantum noise are considered negligible, and an ideal anti-scatter grid (i.e. complete transmission of primary photons and complete rejection of scattered photons) is assumed. Our analysis therefore represents an optimistic estimate of image quality achievable with both DSA and ERA.

2.1 DSA image signal and noise

Digital subtraction angiography requires the subtraction of a post-iodine injection image from a pre-injection (mask) image. For each, the expected signal $d$ from a conventional detector element is proportional to the total energy deposited by the x-ray spectrum incident on the detector:

$$\tilde{d}_i = ak \int_0^{kV} E_0(E) N_0(E) e^{-\int \mu_i(E,x)dx} dE; \quad i = 1, 2$$

where $i = 1$ corresponds to the mask image signal (no contrast agent), $i = 2$ corresponds to the post-contrast-injection signal, $a$ is the area of a detector element, $k$ is a conversion factor converting units of energy to detector units, $\int \mu_i(E, x) dx$ is the line integral of the linear attenuation coefficient along the x-ray path through the
patient, \( N_0(E) \) is the spectrum of x-ray photons incident on the patient \([\text{mm}^{-2}\text{keV}^{-1}]\), and \( E_a(E) \) is the energy absorbed in the detector for an interacting photon having energy \( E \) and is assumed equal to \( E \) under the previously stated assumptions. To a first order approximation, the iodine signal is given by

\[
A_I = -\left( \frac{\mu}{\rho} \right)^{-1} \log \frac{d_2}{d_1} \tag{3}
\]

where

\[
\bar{\mu} = \frac{\int_{0}^{kV} \frac{\mu}{\rho} E_a(E) N_0(E) \, dE}{\int_{0}^{kV} E_a(E) N_0(E) \, dE} \tag{4}
\]

Performing this operation at every pixel in the image gives the spatial distribution of iodine area density in \( \text{g cm}^{-2} \). We calculate the uncertainty in the iodine signal by propagating the error in \( d_1 \) and \( d_2 \) through Eq. (3)\textsuperscript{22-24}

\[
\sigma_I = \sqrt{\sum_{i=1}^{2} \left( \frac{\partial A_I}{\partial d_i} \right)^2 \sigma^2_{d_i} = \left( \frac{\bar{\mu}}{\rho} \right)^{-1} \sqrt{\frac{\sigma^2_{d_1}}{d_1^2} + \frac{\sigma^2_{d_2}}{d_2^2}} \tag{5}
\]

where \( \sigma^2_{d_i} \) is the variance in \( d_i \);

\[
\sigma^2_{d_i} = a^2 k^2 \int_{0}^{kV} E_a^2(E) N_0(E) e^{-\int \mu(E,x)dx} \, dE; \quad i = 1, 2. \tag{6}
\]

Eqs. (3) and (5) are the image signal and noise, respectively, for an iodine-specific angiographic image obtained using a conventional subtraction technique.

### 2.2 ERA image signal and noise

ERA requires only a single post-contrast-injection transmission and the iodine signal is determined from spectral analysis of the data. We model ERA by measuring the energy of each x-ray photon transmitted through a patient and incrementing a counter in the corresponding energy bin for each detector element. We use a two-material decomposition and express the linear attenuation coefficient as a summation of the attenuation coefficients for water and contrast-material:

\[
\int \mu(E, x) \, dx = \sum_{\alpha=1}^{2} \mu_{\alpha}(E) \int \rho(x) \, dx = \sum_{\alpha=1}^{2} \frac{\mu_{\alpha}}{\rho_a}(E) A_{\alpha} = \frac{\mu}{\rho} W(E) A_W + \frac{\mu}{\rho} I(E) A_I \tag{7}
\]

where \( \alpha \) is an index identifying water \((W)\) or iodine \((I)\), and \( A_{\alpha} \) represents the corresponding unknown area density. We require a minimum of two energy bins to estimate \( A_I \) when the line-integral consists of two materials\textsuperscript{8,9,25} as in Eq. (7). Binning the detected spectrum into more then two energy bins will result in lower noise levels in the resulting images.\textsuperscript{26} We therefore apply two energy thresholds: one at the K-edge energy\textsuperscript{26} of iodine and another at an energy greater than the K-edge energy that is chosen to minimize image noise. We let \( \lambda_j \) and \( M_j \) represent the statistical expectation and the actual measured (or Monte Carlo simulation) number of interacting photons in each energy bin, respectively:

\[
\lambda_j(A_I, A_W) = \int_{\tau_j}^{\tau_{j+1}} N_0(E) e^{-\sum_{\alpha=1}^{2} \frac{\mu_{\alpha}(E) A_{\alpha}}{\rho_{\alpha}}} \, dE; \quad j = 1..3 \tag{8}
\]

where \( \tau_j \) and \( \tau_{j+1} \) are the lower and upper energy thresholds for energy bin \( j \). Inspired by Alvarez and Macovski\textsuperscript{26} formalism for dual-energy x-ray imaging, we use a maximum likelihood parameter estimation technique to extract iodine signal from water and bone. This is performed by finding the values of \( A_I \) and \( A_W \) that maximize the likelihood function \( L(A_I, A_W) \), given by\textsuperscript{9,25,27}

\[
L(A_I, A_W) = \prod_{j=1}^{3} \left[ \frac{\lambda_j(A_I, A_W) M_j}{M_j!} \right] e^{-\lambda_j(A_I, A_W)} \tag{9}
\]
The maximum value of \( L(A_I, A_W) \) is obtained when the following relation is satisfied:\textsuperscript{25}

\[
\lambda_j(A_I, A_W) = M_j; \quad j = 1, 3.
\]  \hspace{1cm} (10)

Rather than using a numerical solution to solve Eq. (10), such as that performed by Schomka et al.,\textsuperscript{9} we obtain an approximate analytic solution using a least squares technique developed in the appendix. We evaluate only the contrast-material image and estimate noise in the contrast material signal using the Cramer Rao lower bound for the variance:\textsuperscript{19, 25-27}

\[
\sigma^2_I \geq \mathcal{F}^{-1}_{II}
\]  \hspace{1cm} (11)

where \( \mathcal{F}^{-1} \) is the inverse of the Fischer information matrix which, in this case, is a \( 2 \times 2 \) matrix whose elements are given by\textsuperscript{26}

\[
\mathcal{F}_{\alpha\beta} = \sum_{j=1}^{3} \frac{1}{\lambda_j} \frac{\partial \lambda_j}{\partial A_\alpha} \frac{\partial \lambda_j}{\partial A_\beta}
\]  \hspace{1cm} (12)

where \( \alpha, \beta \in [I, W] \) and

\[
\frac{1}{\lambda_j} \frac{\partial \lambda_j}{\partial A_\beta} = - \int_{\tau_j}^{\tau_{j+1}} \frac{\mu}{\rho} (E) N_0(E) e^{-\sum_{\alpha=1}^{2} \frac{\lambda_{\alpha}}{\lambda_j} (E)} dE
\]

\[
- \int_{\tau_j}^{\tau_{j+1}} N_0(E) e^{-\sum_{\alpha=1}^{2} \frac{\lambda_{\alpha}}{\lambda_j} (E)} dE
\]  \hspace{1cm} (13)

which can be interpreted as the average value of \( \frac{\mu}{\rho} (E) \) weighted by the spectrum of photons incident on the detector. The approximate solution to Eq. (10) gives the iodine signal obtained with ERA and Eq. (11) gives a lower bound for ERA image noise.

### 2.3 Signal-difference-to-noise ratio per unit entrance exposure

We compute the SDNR using in the contrast-specific image using Eq. (1). For both DSA and ERA, \( \sigma_I \) and \( \sigma_0 \) are inversely related to the square root of patient entrance exposure, \( X \), given by\textsuperscript{28}

\[
X = \frac{1}{2.58 \times 10^{-4}} \cdot \int_0^{e} \mu_{en/\rho} (E) \left( \frac{e}{W_{air}} \right) N_0(E) dE
\]  \hspace{1cm} (14)

where \( \mu_{en/\rho} (E) \) is the mean energy transfer coefficient for air in m\(^2\) kg\(^{-1}\), \( (W/e)_{air} = 2.12 \times 10^{17} \) C keV\(^{-1}\) is the mean energy expended in air per ionized electron and 1/\( (2.58 \times 10^{-4}) \) is a conversion factor that converts units of exposure from C kg\(^{-1}\) to roentgens R (1 R = 2.58 \times 10^{-4} C kg\(^{-1}\)). The signal is independent of \( X \) and we therefore consider SDNR per root patient entrance exposure, SDNR/\( \sqrt{X} \), which gives an exposure-independent metric of image quality that can be used to compare DSA and ERA at various applied x-ray tube voltages.

### 3. RESULTS

We applied the above formalism to the task of separating iodinated contrast material from water using polyenergetic x-ray spectra generated by an in-house MATLAB routine that implements algorithms published by Tucker and Barnes\textsuperscript{29} for a tungsten-target x-ray tube. We generated x-ray spectra for applied tube-kV values ranging from 40-105 kV. The spectra were additionally filtered by 2 mm of aluminum. Some representative x-ray spectra are illustrated in Fig. 1.

Fig. 2 shows iodine-image signal difference, noise times root exposure, and SDNR/\( \sqrt{X} \) plotted as a function of applied tube voltage for transmission through 20 g cm\(^{-2}\) of water and 0.02 g cm\(^{-2}\) and 0.05 g cm\(^{-2}\) of iodine for both DSA and ERA, corresponding to 2 and 3-mm thick vessels of 100 mg cm\(^{-3}\) iodine contrast agent. The iodine signal difference, shown in the top plot of Fig. 2, demonstrates that ERA provides similar iodine signal difference to DSA and therefore, in a single x-ray exposure, has DSA-like capability to remove soft-tissue background structures. In general, signal difference tends to decrease as applied tube voltage increases. This effect is, however, modest for both ERA and DSA. Image noise multiplied by square root of exposure is shown in the centre plot of Fig 2. With the exception of very low applied tube voltages (40-45 kV), ERA image noise

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is generally higher than DSA which results in lower SDNR/√X as demonstrated in the lower plot Fig 2. In the case of the high iodine concentration, the best SDNR/√X for DSA is approximately 42 (at 65 kV). In the case of ERA, SDNR/√X reaches a local maximum of 22 at 47 kV followed by a minimum and then a monotonic increase. At 110 kV, SDNR/√X for ERA is approximately 26. In the case of the low iodine concentration, the best SDNR/√X for DSA is approximately 19 (at 62 kV) while for best for ERA SDNR/√X 12. This difference of approximately 1.6 to 2 times is surprisingly small.

Fig. 3 displays signal difference, noise times root exposure, and SDNR per root exposure for DSA and ERA at 70 kV applied tube voltage and 20 and 30 cm of water as a function of iodine area density. The top plot demonstrates that signal difference for both ERA and DSA is linear with iodine area density and that sensitivity to iodine area density is similar for both ERA and DSA. Also, sensitivity shows little dependence on water area density although there is a slight decrease in estimated iodine area density with increasing water thickness for both ERA and DSA - an effect attributable to beam hardening. Image noise, displayed in the middle plot of Fig. 3, does however increase with increasing water area density which results in a large decrease in SDNR/√X for both DSA and ERA. In the case of 20 g cm−2 of water, at very low iodine concentrations (0.005-0.01 g cm−2) DSA is only greater than ERA by a factor of approximately 1.3 to 1.4 times.

4. DISCUSSION

We have demonstrated that energy-resolved x-ray imaging using EPC detectors has the ability to isolate iodine signal in a water-only background. While SDNR for ERA is generally lower than DSA by 30-50%, this technique has the benefit that it only requires a single x-ray exposure where DSA requires multiple exposures. While this technique might not replace DSA in situations where registration of pre and post-injection images is feasible, it may be used to provide DSA-like images when registration is not possible (such as in cardiac imaging). This may provide an exciting opportunity to acquire images of coronary arteries with the background-removed - a task that is currently not possible with DSA.
Figure 2. Plots of iodine-image signal difference (top), noise times root exposure (center), and SDNR/√X (bottom) as a function of tube voltage for both DSA and ERA for transmission through 20 cm of water and selected area densities of iodine.
Figure 3. Plots of iodine-image signal difference (top), noise (center), and $\text{SDNR}/\sqrt{X}$ (bottom) as a function of iodine area density for both DSA and ERA for transmission through 20 cm and 30 cm of water acquired at 70 kV.
Our results demonstrate that it may be possible to perform ERA at lower applied tube voltages than DSA without sacrificing image quality which would result in lower dose for the same x-ray exposure. This added benefit of ERA is, however, not reflected in the comparison presented here because we used SDNR/$\sqrt{X}$ as a figure of merit. This figure of merit does not reflect the real risks to patients being exposed to ionizing radiation and SDNR per root effective dose may be a more appropriate metric and would also make ERA compare more favorably with DSA.

In this study, we assumed ideal x-ray detectors (where all incident photons interact and all the energy of each interacting photon is deposited) were used for both DSA and ERA. However, random processes such as the production, real absorption, and escape of characteristic and Compton scatter x rays in a detector result in variations in deposited photon energy. It has been known for some time that these processes degrade the detective quantum efficiency (DQE) of conventional x-ray detectors$^{30-34}$ and has been shown more recently that they also affect the accuracy and precision of energy measurements in EPC detectors.$^{17}$ These limitations are widely recognised by many researchers and methods are being implemented in prototypes such as the Medipix-3 to overcome them.$^{16,18}$ While these factors will degrade ERA image quality they will also degrade DSA image quality and the relative effects on both requires further study.

5. CONCLUSIONS

X-ray imaging using ideal energy-resolving photon-counting detectors has the potential to provide DSA-like angiographic images of iodinated vasculature in a single x-ray exposure, therefore eliminating motion-related image artifacts that limit the use of DSA in cardiac applications. ERA may potentially be used in for background removal in situations where DSA cannot be used, such as in cardiac imaging.

6. APPENDIX

Material-separation technique

The solution to the maximum likelihood problem is obtained when the equality in Eq. (10) is satisfied. We seek here and approximate analytic solution to this system of three equations in two unknowns. Dividing the left side of Eq. (10) by $m_j = \int_{\tau_j}^{\tau_{j+1}} N_0(E) \, dE$ and taking the logarithm results in

$$- \log \frac{\int_{\tau_j}^{\tau_{j+1}} N_0(E) \, e^{-\sum_{\alpha=1}^{2} \frac{1}{\rho \alpha(E) A_{\alpha}} \, dE}}{\int_{\tau_j}^{\tau_{j+1}} N_0(E) \, dE} = - \log \frac{M_j}{m_j}$$

(15)

Replacing the left side of the above equation with its first order Taylor series gives

$$- \log \frac{\int_{\tau_j}^{\tau_{j+1}} N_0(E) \, e^{-\sum_{\alpha=1}^{2} \frac{1}{\rho \alpha(E) A_{\alpha}} \, dE}}{\int_{\tau_j}^{\tau_{j+1}} N_0(E) \, dE} \approx 1 - \frac{\int_{\tau_j}^{\tau_{j+1}} N_0(E) \, e^{-\sum_{\alpha=1}^{2} \frac{1}{\rho \alpha(E) A_{\alpha}} \, dE}}{\int_{\tau_j}^{\tau_{j+1}} N_0(E) \, dE}.$$  

(16)

Replacing the exponentials with their first order Taylor series gives$^{35}$

$$- \log \frac{\int_{\tau_j}^{\tau_{j+1}} N_0(E) \, e^{-\sum_{\alpha=1}^{2} \frac{1}{\rho \alpha(E) A_{\alpha}} \, dE}}{\int_{\tau_j}^{\tau_{j+1}} N_0(E) \, dE} \approx \sum_{\alpha=1}^{2} \frac{\mu}{\rho j \alpha A_{\alpha}}.$$  

(17)

where

$$\frac{\mu}{\rho j \alpha} = \frac{\int_{\tau_j}^{\tau_{j+1}} \frac{\mu}{\rho \alpha} \, (E) \, N_0(E) \, dE}{\int_{\tau_j}^{\tau_{j+1}} N_0(E) \, dE}.$$  

(18)
Therefore
\[ \sum_{\alpha=1}^{2} \bar{\mu}_{j\alpha} A_{\alpha} = -\log \frac{M_j}{m_j} \]  

(19)

The above relationship is a system of three linear equations in the unknown area densities \( A_{\alpha} \). This is a system of three equations in two unknowns and therefore has no solution. We obtain an approximate solution using a least squares technique.

**REFERENCES**


