A theoretical comparison of x-ray angiographic image quality using energy-dependent and conventional subtraction methods

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Purpose: X-ray digital subtraction angiography (DSA) is widely used for vascular imaging. However, the need to subtract a mask image can result in motion artifacts and compromised image quality. The current interest in energy-resolving photon-counting (EPC) detectors offers the promise of eliminating motion artifacts and other advanced applications using a single exposure. The authors describe a method of assessing the iodine signal-to-noise ratio (SNR) that may be achieved with energy-resolved angiography (ERA) to enable a direct comparison with other approaches including DSA and dual-energy angiography for the same patient exposure.

Methods: A linearized noise-propagation approach, combined with linear expressions of dual-energy and energy-resolved imaging, is used to describe the iodine SNR. The results were validated by a Monte Carlo calculation for all three approaches and compared visually for dual-energy and DSA imaging using a simple angiographic phantom with a CsI-based flat-panel detector.

Results: The linearized SNR calculations show excellent agreement with Monte Carlo results. While dual-energy methods require an increased tube heat load of 2 to 4 compared to DSA, and photon-counting detectors are not yet ready for angiographic imaging, the available iodine SNR for both methods as tested is within 10% of that of conventional DSA for the same patient exposure over a wide range of patient thicknesses and iodine concentrations.

Conclusions: While the energy-based methods are not necessarily optimized and further improvements are likely, the linearized noise-propagation analysis provides the theoretical framework of a level playing field for optimization studies and comparison with conventional DSA. It is concluded that both dual-energy and photon-counting approaches have the potential to provide similar angiographic image quality to DSA. © 2012 American Association of Physicists in Medicine. [DOI: 10.1118/1.3658728]

Key words: angiography, dual-energy, energy-resolved, photon-counting, iodine imaging

I. INTRODUCTION

Cardiovascular diseases (CVDs) are the leading causes of death worldwide. In 2004, an estimated 17.1 million people died from CVDs, representing 29% of all global deaths. Of these, an estimated 7.2 million were due to coronary heart disease (CHD) and 5.7 million to stroke. Accurate imaging of CVD patients is critical for clinical decision making such as guiding and planning surgical interventions, where disease classification requires arterial lesions be categorized based on length and location. Carotid luminal stenoses can be an indicator of an unstable (“vulnerable”) plaque with increased risk of thrombosis and stroke.

Investigations for diagnosis and treatment planning may include x-ray digital subtraction angiography (DSA), magnetic resonance angiography (MRA), computed tomography angiography (CTA), or duplex ultrasonography (DU). DU is often used as a screening tool and follow-up DSA, CTA, or MRA investigations are usually performed to confirm diagnosis and plan surgical interventions. CTA and MRA are seen to be increased due to improvements in spatial and temporal resolution made over the past decade. In spite of these great advances, DSA, developed over two decades ago, remains the reference standard for imaging near-stationary vasculature such as the peripheral and the neurovasculature. With this technique, an image acquired prior to injection of an iodinated contrast agent is subtracted from a series of postinjection images, thereby largely removing overlapping anatomical structures. However, the need for both preinjection and postinjection exposures, often
many seconds apart, can result in severe motion artifacts and failed or compromised diagnostic procedures. 16

Although large movements during image acquisition are largely avoided with a cooperative patient, respiratory and cardiac motions are common. Involuntary motions such as swallowing after a carotid injection can impair image quality 16–18 and movement of extremities can degrade visualization of peripheral arteries. 19,20 In coronary angiography, subtraction methods are almost never employed, and high quality images are obtained using a relatively high radiation exposures and iodine concentrations to ensure that both large and small arteries are clearly distinguished over background structures. Image processing techniques have been helpful for retrospective registration, particularly for simpler motions. 21–23

An alternative approach may come from the development of a new generation of x-ray detectors capable of estimating the energy of each interacting x-ray photon. An exciting aspect of energy-resolved photon-counting (EPC) imaging is the potential to generate “DSA-like” images from a single exposure that are not susceptible to motion artifacts. Energy-resolved angiography (ERA) would use measurements of the spectrum of interacting x-ray energies in each pixel to estimate the iodine attenuation along each path. 24,25

Many technical barriers must be overcome before EPC detectors are ready for use in ERA. For example, they must operate at very high count rates that cannot be achieved at present. In addition, angiography requires high spatial resolution but the use of small detector elements will result in reabsorption of characteristic and Compton-scatter x rays and therefore charge sharing in near-by elements. This may result in increased image noise, 26–33 although fast coincidence detection algorithms, such as that implemented in the Medipix-3 prototype detector, 29 may prevent these effects.

Another approach, originally proposed in the 1980s, is the use of dual-energy methods to produce an iodine-specific image 19,34–38 based on two (or more) x-ray images acquired at different average energies to enhance or suppress materials of a particular atomic number. 39–41 While not in use at present, energy-subtraction angiography (ESA) could be implemented using fast kV-switching to generate DSA-like images with reduced or eliminated motion artifacts.

While early dual-energy studies suggested that iodine signal-to-noise ratio (SNR) would be much less than that of DSA (by a factor of 2–5), 36,37,42,43 these studies did not specifically address whether reduced SNR was a result of technological limitations or the fundamental physics of dual-energy imaging. For example, early dual-energy cardiac studies used smaller x-ray tubes with low heat capacity that forced operation at lower patient exposures and could not control exposure times independently. These limitations resulted in decreased SNR but may be less restrictive at present.

While ERA and ESA are exciting alternatives, their potential success depends largely on the image quality that can be achieved for a given exposure (or effective dose) to the patient. In this paper, we use linearized expressions of image signal and noise to develop a theoretical framework to enable this comparison, with the unexpected result that both ERA and ESA have the potential to produce similar image quality to DSA.

II. THEORY

We consider the task of isolating contrast agents (iodine) embedded in a soft-tissue and/or bony environment. The goal is to produce an image showing only the spatial distribution of the contrast agent. The attenuation of x rays through a patient is determined from the line integral of the linear attenuation coefficient $\mu(s; E)$ along the x-ray path, which we express as a linear combination of basis-material mass-attenuation coefficients: 24,40,44,45

$$\mu(s; E)ds = \sum_{b=1}^{m} \frac{\mu_{s}}{\rho_{s}}(E)A_{b} = A^{T} \frac{\mu}{\rho}(E),$$

where $b$ identifies the basis material, $m$ is the number of basis materials, $s$ represents position along the x-ray path as shown in Fig. 1, and $E$ is the photon energy.

$$A = \begin{bmatrix} A_{1} \\ \vdots \\ A_{m} \end{bmatrix} \quad \text{and} \quad \frac{\mu}{\rho}(E) = \begin{bmatrix} \frac{\mu_{s}}{\rho_{s}}(E) \\ \vdots \\ \frac{\mu_{n}}{\rho_{n}}(E) \end{bmatrix}.$$  

The coefficients of the expansion, $A_{b}$, represent the area densities of each basis material such as soft-tissue ($A_{S}$), bone ($A_{B}$), and iodine ($A_{I}$). The mass-attenuation coefficients of possible basis materials are shown in Fig. 2. An image showing any of the basis materials can be generated by estimating $A$ at each pixel location. In the following subsections, we provide a general mathematical formalism for estimating $A$ from x-ray transmission measurements acquired using either energy-integrating or photon-counting x-ray detectors. We use an overall tilde (e.g., $\tilde{x}$) to represent random variables (RVs) and $E\{\tilde{x}\}$, $\text{Var}\{\tilde{x}\}$, and $\text{Cov}\{\tilde{x}, \tilde{y}\}$ to represent the expected value, variance, and covariance, respectively.

II.A. Angiographic image signal

The angiographic image signal $A_{I}$ is derived from two or more images where, for linear detectors, the expected pixel value measured in image $i$, is given by

$$E\{\tilde{M}_{i}\} = k \int_{0}^{dV_{i}} S_{i}(E)\tilde{q}_{i}(E)e^{-A_{I}^{T}\frac{\mu_{b}(E)}{\rho_{b}}(E)}dE; \quad i = 1 \ldots n,$$

where $k$ is a constant of proportionality, $\tilde{q}_{i}(E)$ and $dV_{i}$ describe the spectral distribution of x-ray photons incident on the patient (mm$^{-2}$ keV$^{-1}$) corresponding to image $i$, and $S_{i}(E)$

![Fig. 1. Schematic showing x-ray paths through iodinated and background regions of a patient for the incident spectrum $\tilde{q}_{b}(E)$.](image-url)
is a weighting function describing the detector response associated with image $i$. The form of $S(E)$ requires some explanation. For a conventional detector that produces a single image with a signal proportional to absorbed energy, $S(E) = \alpha(E)E_{\text{phot}}(E)$, where $\alpha$ and $E_{\text{phot}}$ are the detector quantum efficiency and absorbed energy, respectively, for a photon of energy $E$. For an ideal photon counting detector, $S(E) = \alpha(E)$ for energies within bin $i$ and is zero otherwise. For the dual-energy approach, $n = 2$ and $S_i(E)$ corresponds to the conventional detector described above where $i$ indicates the spectrum.

Attenuation of the spectral distribution of x-rays $\tilde{q}_i(E)$ through a patient is determined from the log signal, $\tilde{l}_i$, given by

$$\tilde{l}_i = -\log\frac{M_i}{M_{0i}}; \quad i = 1 \ldots n,$$

where $M_i/M_{0i}$ is an image of x-ray transmission values and $M_{0i}$ is the image corresponding to no patient. The above relationship represents a system of $n$ nonlinear equations in the $m$ unknowns $A_1, \ldots, A_m$. The solution to Eq. (4) provides an estimate of the area density of each basis material. However, in general, Eq. (4) has no analytic solution. We apply a simple linearization technique similar to Le and Molloi and Cardinal and Fenster to obtain an approximate analytic solution. We let $A_0 = [A_{01}, \ldots, A_{0m}]$ represent the point about which we expand the log signal $\tilde{l}_i$ and $\tilde{l}_{0i} = \tilde{l}_i|_{A=A_0}$. In Appendix, we show that the linearized version of Eq. (4) about $A = A_0$ is given by

$$\mathbf{L} - \mathbf{L}_0 = \mathbf{J}(\mathbf{A} - \mathbf{A}_0),$$

where

$$\mathbf{L} - \mathbf{L}_0 = \begin{bmatrix} \tilde{l}_1 - \tilde{l}_{01} \\ \vdots \\ \tilde{l}_n - \tilde{l}_{0n} \end{bmatrix},$$

and $\mathbf{J}$ is the Jacobian matrix with elements given by

$$J_{ib} = \frac{\partial}{\partial A_{0b}} \tilde{l}_i; \quad i = 1 \ldots n, \quad b = 1 \ldots m,$$

where $\partial \tilde{l}_i/\partial A_{0b}$ denotes the average value of the mass-attenuation coefficient of basis material $b$ weighted by $S_i(E)\tilde{q}_i(E)e^{-A_{0i}E}$.

In practice, $\mathbf{L}_0$ could be determined from either theoretical calculations or a series of calibration scans. Equation (5) has a unique solution for $n = m$ and no solution for $n > m$, which occurs, for example, when using EPC x-ray detectors with more energy bins than basis materials. In the latter case, we use a simple least-squares technique similar to that of Le and Molloi. The estimated area-density vector is then expressed as

$$\mathbf{A} = \mathbf{A}_0 + \mathbf{W}(\mathbf{L} - \mathbf{L}_0),$$

where

$$\mathbf{W} = \begin{cases} \mathbf{J}^{-1} & \text{for } n = m \\ (\mathbf{J}^\top \mathbf{J})^{-1} \mathbf{J}^\top & \text{for } n > m. \end{cases}$$

Equations (9) and (10) give an estimate of the area density of each basis material for all three techniques considered in this study. They may also be used to determine area densities from hybrid detectors that use some combination of energy-resolving, photon-counting, and energy-integrating measurements, such as described by Alvarez. For $\mathbf{A}_0 = \mathbf{0}$, this result is equivalent to commonly used expressions for linear dual-energy, temporal-subtraction, and energy-resolved approaches. An angiographic image is obtained by solving for the iodine-specific signal $\tilde{A}_1$.

II.B. Angiographic image noise

Random variations in the number of interacting photons, the energy deposited by each photon, and the number of secondary quanta collected in a detector element will result in random variations in $\tilde{l}_i$ and therefore noise in the material-specific images. Roessl et al. and Wang and Pelc both used error-propagation techniques and the Cramér–Rao lower bound to estimate large-area basis-image noise for EPC detectors. In this paper, we generalize the error-propagation approach used by Roessl et al. to describe the signal-to-noise ratio in basis-material images for both energy-integrating and EPC detectors to allow for a direct comparison of image SNR.

The covariance matrix of the basis-material images $\mathbf{V}(\mathbf{A})$ is related to the covariance matrix of the log signals $\mathbf{V}(\mathbf{L})$ by

$$\mathbf{V}(\mathbf{A}) = \mathbf{WV}(\mathbf{L})\mathbf{W}^\top,$$

where $\mathbf{W}$ is given by Eq. (10) and

$$V_{ij}(\mathbf{L}) = \begin{cases} \text{Cov}\{\tilde{l}_i, \tilde{l}_j\} & \text{for } i \neq j \\ \text{Var}\{\tilde{l}_i\} & \text{for } i = j \end{cases},$$

with a similar result for $\mathbf{V}(\mathbf{A})$.

We separate our analysis of basis-image noise into two cases, corresponding to independent and cross-correlated measurements $\tilde{M}_i$. While in most cases $\tilde{M}_i$ will correspond to
independent measurements and will therefore be statistically uncorrelated, cross correlations may occur when, for example, an x-ray detector records both the total energy deposited and the total number of photons interacting in a detector element from the same exposure. Note that these correlations are not spatial correlations within a single image—they are cross correlations between the two or more measurements used to derive $A$.

II.B.1. General case: Cross-correlated measurements

In Appendix, we show that

$$\text{Cov}\{\tilde{I}_i, \tilde{I}_j\} = \frac{\text{Cov}\{\tilde{M}_i, \tilde{M}_j\}}{\text{E}\{\tilde{M}_i\} \text{E}\{\tilde{M}_j\}}.$$  \hfill (13)

and

$$\text{Var}\{\tilde{I}_i\} = \frac{\text{Var}\{\tilde{M}_i\}}{\text{E}\{\tilde{M}_i\}^2} = \frac{1}{\text{SNR}_{\text{M}}^2},$$  \hfill (14)

where SNR$_{\text{M}}$ represents the SNR for $\tilde{M}_i$. The analytical form of $\text{Var}\{\tilde{M}_i\}$ has been extensively described in the literature, for example, see Swank$^{53}$ or Alvarez and Macovski.$^{44}$

For each of the three methods considered in this paper $\text{Cov}\{\tilde{M}_i, \tilde{M}_j\} = 0$. We refer the interested reader to Roessl$^{41}$ or Alvarez$^{47}$ for details on calculating $\text{Cov}\{\tilde{M}_i, \tilde{M}_j\}$ in the case that it is nonzero.

Combining Eqs. (11)–(14), the covariance between material-specific images for basis materials $b$ and $b'$ is given by

$$V_{bb'}(A) = \sum_{i=1}^{n} \sum_{j=1}^{n} W_{ij} \text{Cov}\{\tilde{M}_i, \tilde{M}_j\} W_{ji} \frac{1}{\text{E}\{\tilde{M}_i\} \text{E}\{\tilde{M}_j\}}.$$  \hfill (15)

The above equation gives the variance $(b = b')$ and covariance $(b \neq b')$ of the material-specific images for the general case of cross-correlated measurements $\tilde{M}_i$.

II.B.2. Special case: Independent measurements

For the case of independent measurements $\tilde{M}_i$, $\text{Cov}\{\tilde{M}_i, \tilde{M}_j\} = \delta_{ij} \text{Var}\{\tilde{M}_i\}$, where $\delta_{ij}$ is the Kronecker delta equal to one for $i = j$ and zero otherwise. Therefore,

$$V_{bb'}^{\text{indep}}(A) = \sum_{i=1}^{n} W_{ii} W_{ji} \frac{1}{\text{SNR}_{\text{M}}^2}.$$  \hfill (16)

The above equation gives the variance and covariance of basis-material estimates when the measured (raw) image signals $M_i$ and $M_j$ are statistically independent, including the three methods compared in this paper. This calculation accommodates cross-correlations between material-specific images as described by the $b \neq b'$ case, such as may occur with dual-energy methods or between calcium and soft-tissue images using EPC detectors as described by Wang and Pelc.$^{32,33,52}$

II.C. Iodine detectability

The ability to visualize iodinated vasculature is related to the iodine signal-difference-to-noise ratio (SDNR), and this ratio is different for each of the methods compared in this work. We compare the three methods in terms of a performance metric related to the detectability index,$^{54}$ defined as the iodine SDNR per square-root of patient entrance exposure

$$P_i = \frac{\text{SDNR}_I}{\sqrt{X}} = \frac{1}{\sqrt{X}} \frac{\text{E}\{\tilde{A}_I - \tilde{A}_I^N\}}{\sqrt{\text{Var}\{\tilde{A}_I - \tilde{A}_I^N\}}}.$$  \hfill (17)

where $X$ is the patient entrance exposure.$^{55}$ and $\tilde{A}_I$ and $\tilde{A}_I^N$ are the iodine signals from iodinated and noniodinated regions of the images, respectively. In this study, we ignore spatial correlations in an image, in which case

$$\sqrt{\text{Var}\{\tilde{A}_I - \tilde{A}_I^N\}} = \sqrt{\text{Var}\{\tilde{A}_I\} + \text{Var}\{\tilde{A}_I^N\}}.$$  

III. METHODS AND MATERIALS

III.A. Theoretical comparison of energy-resolved, energy-subtraction, and digital-subtraction angiography

The method described above was used to theoretically compare image quality that can be obtained with each of the three methods for the same exposure. For each method, we consider the task of isolating iodine embedded in water. In all cases, our model assumes ideal energy resolution and unity quantum efficiency. Nonideal energy resolution will likely increase the variance of basis-material estimates for each of the techniques considered. This effect may be more pronounced in the case of ERA, where nonideal energy resolution may result in “cross-talk” (correlations) between energy bins. All sources of noise apart from Poisson quantum noise are considered negligible, and an ideal anticscatter 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 each method.

In the following sections, all x-ray spectra are generated using an in-house MATLAB routine that implements algorithms published by Tucker$^{56}$ for a tungsten-target x-ray tube.

III.A.1. DSA

DSA requires subtraction of a postinjection image from a preinjection (mask) image. For each, the expected signal from a conventional energy-integrating detector element is proportional to the total energy deposited by the x-ray spectrum incident on the detector

$$E\{\tilde{M}_{\text{pre}}\} = k \int_{0}^{4k} E \tilde{q}(E) e^{-\int_{0}^{4k} E \tilde{q}(E) A_w dE} dE,$$  \hfill (18)

$$E\{\tilde{M}_{\text{post}}\} = k \int_{0}^{4k} E \tilde{q}(E) e^{-\int_{0}^{4k} E \tilde{q}(E) A_w - \int_{0}^{E} \tilde{q}(E) A_I dE} dE,$$  \hfill (19)

where $A_w$ is the area density of water. We theoretically calculated image signal [Eqs. (9) and (10)], noise [Eq. (16)], and $P_i$ [Eq. (17)] for applied-tube voltages ranging from 50 to 150 kV with an additional 2 mm of aluminum filtering.
III.A.2. ESA

We consider a dual-energy approach that makes use of two postinjection images with different high and low average energies to isolate the iodine signal from background

\[
E\{M_L\} = k \int_{0}^{\text{E}_{L}} E q_L(E) e^{-\mu_{L}(E)A_{L}} dE, \quad (20)
\]

\[
E\{M_H\} = k \int_{0}^{\text{E}_{H}} E q_H(E) e^{-\mu_{H}(E)A_{H}} dE. \quad (21)
\]

Previous studies suggest that optimal SNR is obtained when the low-energy applied-tube voltage is in the range of 50–60 kV and the high energy applied-tube voltage is in the range of 100–130 kV.37,42 These studies also suggest that filtering the high-energy applied-tube voltage with and addition 2–2.5 mm of copper (Cu) provides optimal SNR. We, therefore, fixed the low-energy applied-tube voltage at 50 kV and varied both the high-energy applied-tube voltage and low-to-high-energy mAs ratio to maximize P_I. For each spectral combination, both the low and high-energy spectra were filtered with 2 mm of Al with an additional 2.1 mm of Cu on the high energy spectrum. For each combination of exposure parameters, the theoretical technique developed in Sec. II was used to calculate image signal, noise, and P_I.

III.A.3. ERA

ERA requires only a single postcontrast-injection transmission and binning of x-ray photons into prespecified energy bins to isolate the iodine signal from background. The signal from each energy bin is given by

\[
E\{M_i\} = k \int_{E_{i-1}}^{E_i} q(E) e^{-\mu(E)A_{L}} dE; \quad i = 1...n, \quad (22)
\]

where \(n\) is the number of energy bins. We calculated image signal and noise for 2 and 3-bin ERA approaches (using a least-squares solution for the 3-bin method). For both approaches, we varied the applied-tube voltage from 50 to 150 kV and applied a numerical optimization using MATLAB’s pattern search function to determine the location of the energy thresholds that maximize P_I. For each combination of exposure parameters, the theoretical technique developed in Sec. II was used to calculate image signal, noise, and P_I.

III.B. Monte Carlo validation

The theoretical formalism developed in Sec. II was validated with a simple Monte Carlo calculation. The number of incident x-ray photons in each energy interval (1 keV) was determined for the desired exposure using a Poisson random number generator. A virtual phantom with iodine area densities of 0, 10, 20, 30, 40, and 50 mg cm\(^{-2}\) embedded in 20 cm of water was used for numerical comparison with theoretical results. A second virtual phantom consisting of iodinated vasculature with diameters of 0.2–0.5 cm filled with 0.10 g cm\(^{-3}\) of iodine embedded in 20 cm of water with an extra 2 cm of water placed over the right half of the image was used to compare the background removal capabilities of each technique. For each virtual phantom, a 128 × 128 grid of 0.2 × 0.2-mm detector elements was simulated, giving a 2.56 × 2.56-cm image. Transmissions were calculated using tabulated values of the mass-attenuation coefficients for water and iodine. For each technique, we used the exposure parameters (summarized in Table I) that maximized P_I.

To simulate energy-integrating images, we weighted each transmitted x-ray photon by its energy and then summed over the entire spectral distribution. To simulate EPC images, we summed the number of transmitted photons between the lower and upper energy thresholds for each energy bin. Iodine-specific images for DSA, ESA, and ERA were then generated using the contrast separation technique developed in Sec. II.

III.C. Visual comparison of ESA with DSA

A visual comparison of ESA with DSA was obtained experimentally using a simple static vascular phantom consisting of two tubes of variable inner diameters (steps of 0.15, 0.4, and 0.8 cm) filled with 0.10 g cm\(^{-3}\) of iodine. The tubes were placed in 20 cm of water with an extra thickness of 2.5 cm of poly(methyl methacrylate) (PMMA) placed over the left tube to provide background (noniodinated) contrast.

We acquired a series of contrasted and mask images (with and without the tubes). For the ESA experiment, we also acquired open-field images at both kV values required for the log-transform in Eq. (4). Ten open-field images were acquired (at lower mAs values to prevent detector saturation and then scaled to match the mAs of the contrast images) and averaged. The contrast separation technique developed in Sec. II was then used to generate iodine-specific images for both DSA and ESA. In all cases, we linearized the image signals about zero water thickness. We were unable to perform an ERA experiment because our laboratory currently does not have access to an EPC x-ray detector.

All images were acquired using a General Electric Revolution XR d x-ray system with a 1 m source-image distance. This system uses a conventional x-ray tube (General Electric MX-100, General Electric Medical Systems) and generator (General Electric SCPU-80, General Electric Medical Systems) with a CsI based flat-panel detector. Exposure parameters are shown in Table II.

### Table I. Exposure parameters used for the Monte Carlo study.

<table>
<thead>
<tr>
<th>Imaging technique</th>
<th>DSA</th>
<th>ERA</th>
<th>ESA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Applied-tube voltage (kV)</td>
<td>63</td>
<td>150</td>
<td>50/130</td>
</tr>
<tr>
<td>Al filtration per image (mm)</td>
<td>2/2</td>
<td>2</td>
<td>2/2</td>
</tr>
<tr>
<td>Cu filtration per image (mm)</td>
<td>0/0</td>
<td>0</td>
<td>0/2.1</td>
</tr>
<tr>
<td>Tube current per image (mAs)</td>
<td>9.25/9.25</td>
<td>3</td>
<td>28.5/11.1</td>
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<tr>
<td>Heat units (mAs × kV)</td>
<td>1166</td>
<td>450</td>
<td>2733</td>
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<tr>
<td>Entrance exposure per image (mR)</td>
<td>20/20</td>
<td>40</td>
<td>28.7/11.3</td>
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</tbody>
</table>

IV. RESULTS

IVA. Dependence on imaging parameters

IVA.1. Exposure technique

Figure 3 illustrates the dependence of iodine signal, noise × \(\sqrt{X}\), and the performance metric P_I for each of the three
methods on exposure parameters for 20 cm of water and 20 mg cm\(^{-2}\) of iodine. In all cases, the log signals were expanded about 20 cm of water. In general, there is little variation in signal with variable exposure parameters for each of the three techniques.

In the case of DSA, the performance metric reaches a maximum when the applied-tube voltage is approximately equal to 63 kV. This is consistent with previous studies. See, for example, Gkanatsios et al.\(^{57}\) Preinjection and postinjection x-ray spectra for 20 cm of water and 40 mg cm\(^{-2}\) of iodine are illustrated in Fig. 4 for a 40 mR entrance exposure.

In the case of ERA, there is little difference in PI between the 2 and 3-bin approaches. This is consistent with the findings of Shikhaliev\(^{58}\) who demonstrated that there is little change in iodine contrast-to-noise ratio (CNR) between 2 and 5-bin approaches. For both approaches, iodine SNR reaches a minimum when the applied-tube voltage is in the range of 55–65 kV and then increases with increasing applied-tube voltage. Because there is little difference between the 2 and 3-bin approaches, from this point forward, we present the results of the 2-bin approach in comparison with ESA and DSA. We used a 150 kV applied-tube voltage with an energy threshold at 59 keV which was determined to be optimal and is consistent with that found by Nik et al.\(^{59}\) The postinjection transmitted x-ray spectrum is illustrated in Fig. 4 for a 40 mR entrance exposure.

In the case of ESA, applied-tube voltages of 50–130 kV (with the high-energy spectrum additionally filtered by 2.1 mm of Cu) with a low-to-high-energy mAs ratios of 2.3 provided the highest SNR of the spectral combinations considered. These parameters are similar to those used in previous studies.\(^{37,42}\) Postinjection high and low-energy spectra are illustrated in Fig. 4 for a 40 mR entrance exposure.

### IV.A.2. Taylor-expansion point

Figure 5 illustrates the dependence of iodine signal and PI on the Taylor-expansion point \(A_0 = [A_{I0}, A_{W0}]\) for 20 cm of water and iodine concentrations of 20 mg cm\(^{-2}\) and 50 mg cm\(^{-2}\) of iodine. In all cases, we expanded about \(A_{I0} = 0\). In general, iodine signal becomes more inaccurate as the expansion point increases or decreases from the true area densities for all three techniques. This effect could likely be reduced by using more energy bins in the ERA approach. While the image signals show variation with expansion point, PI for all three techniques shows very little dependence on \(A_{W0}\). In the case of DSA, PI is independent of \(A_{W0}\). For all remaining theoretical and simulation results presented, the log signals were expanded about 20 cm of water.

### IV.A.3. Iodine concentration

Iodine-specific images, generated using the exposure parameters in Table I for various iodine concentrations in 20 cm of water, are shown in Fig. 6. The iodine signal \(A_I\) for each concentration is given by the pixel value in these images. The iodine signal and performance metric PI, determined using Eq. (17) is compared with theoretical predictions in Fig. 7. Excellent agreement was obtained between our theoretical method and the Monte Carlo calculations.

All three methods show a linear response with near-unity slope with increasing iodine concentration as illustrated in the upper plot of Fig. 7. Surprisingly, for this particular choice of exposure parameters, the performance metric PI for ESA is slightly higher than that of ERA and both are within 5%–10% of DSA under these conditions.

### IV.A.4. Water thickness

The upper plot of Fig. 8 demonstrates that there is little variability in iodine signal with increasing water thickness for each of the three methods. However, as described earlier, as the actual water thickness increases or decreases from the

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Applied-tube voltage (kV)</td>
<td>63/50/130</td>
<td>50/0/210</td>
</tr>
<tr>
<td>Cu filtration per image (mm)</td>
<td>0/0/0</td>
<td>0.2/0/0</td>
</tr>
<tr>
<td>Tube current per image (mAs)</td>
<td>4/4/4</td>
<td>10/4</td>
</tr>
<tr>
<td>Heat units (mAs × kV)</td>
<td>504/1020</td>
<td>1020/1020</td>
</tr>
<tr>
<td>Entrance exposure per image (mR)</td>
<td>9/9</td>
<td>11/4/11</td>
</tr>
</tbody>
</table>

FIG. 4. Dependence of iodine SNR on exposure parameters. The top row illustrates the dependence of DSA and ERA on the applied-tube voltage. The bottom row illustrates the dependence of ESA on both the high-energy applied-tube voltage and the low-to-high-energy mAs ratios.
expansion point \( A_0 = [0, 20] \)) the signals become slightly inaccurate.

The lower plot of Fig. 8 shows that all three methods have similar PI values over a wide range of water thickness values, although DSA is slightly better below 20 cm. However, it must be emphasized that the spectral methods shown here are not necessarily optimized and may be improved further. The important observation is to note how similar they are to each other.

**IV.B. Background suppression**

The ability of each method to suppress (noniodinated) background structures is illustrated in Fig. 9 where an extra 2 cm of water was placed in the right half of each image in the Monte Carlo calculation. All three methods show excellent suppression with only minor noise modulation caused by reduced x-ray transmission through the additional water thickness.

**IV.C. Visual comparison of ESA with DSA**

Experimental DSA and ESA images are shown in Fig. 10. The background PMMA structure has been effectively removed and a series of very small air bubbles, adhering to the top section of each vessel, appear as increased brightness in the DSA image but do not appear at all in the ESA image (ESA is a true iodine-specific method). The ESA image appears slightly noisier than the DSA image for two reasons: (1) the x-ray exposure used to acquire the ESA image was 17% lower than that used to acquire the DSA image; and (2) the ESA method requires an open-field image to determine \( M_0 \) as described in Sec. III C and an insufficient number of images were averaged (10 at a reduced mAs) to avoid adding noise to the iodine image. In practice, it would be necessary to average a large number of open images (no patient) to ensure maximal iodine SNR.

**V. DISCUSSION**

Energy-resolved and energy-subtraction angiography are exciting alternatives to DSA and their potential success depend largely on the image quality that can be achieved for a given exposure (or effective dose) to the patient. We have presented a theoretical framework for such a comparison based on linear estimates of basis-material area densities. It is sufficiently general to include either energy-integrating or energy-resolving photon-counting x-ray detectors, or a combination such as that described by Alvarez.47

Fig. 4. X-ray spectra for DSA, ERA, and ESA. The preinjection DSA spectrum has been transmitted through 20 cm of water and all postinjection spectra have been transmitted through 20 cm of water and 40 mg cm\(^{-2}\) of iodine. The total entrance exposure for each spectral combination is 40 mR.
While the tube heat load for ESA was higher than that of DSA by $2 \times 4$, and photon-counting detectors are not yet ready for angiographic imaging, the available iodine SNR for both methods as tested is within 10% of that of conventional DSA for the same patient exposure over a wide range of patient thicknesses and iodine concentrations. This was an unexpected result as it is generally regarded that image quality (iodine SNR) obtained with ESA is less than that of DSA. Early dual-energy studies may have suffered from technological limitations that are less of an issue now.

It must also be noted that the results shown here apply only to the methods as tested. There may be alternative approaches that could improve each method, such as increasing the number of energy bins used for decomposition in ERA, or using a weighted linear least-squares approach to estimate iodine signal that takes into consideration the statistics of the energy bins. Also, while the linearized methods compared in this study are commonly used in energy-subtraction, temporal-subtraction, and energy-resolved approaches, we have not compared nonlinear iterative methods such as those of Lehmann et al. and Schlomka et al. Suppression of more than one material (such as bone and soft-tissue) might require additional images for ESA or energy bins for ERA and likely reduce SNR but has not been compared.

For each technique considered in this study, we assumed ideal x-ray detector technology for both theoretical and simulation studies. For example, in the case of ERA, pulse pile up will likely reduce SNR but was not considered. In addition, the random processes of x-ray interactions (e.g., conversion to secondary quanta, characteristic escape, etc.) that degrade the detective quantum efficiency (and SNR) of all x-ray detectors will reduce image quality for DSA, ESA, and ERA and have not been addressed.
VI. CONCLUSIONS

The linearized noise-propagation analysis described here provides a framework for optimizing and evaluating iodine SNR that may be obtained using novel energy-based methods. Using this framework, energy-resolved photon-counting angiography and dual-energy angiography were compared with conventional digital-subtraction angiography. Theoretical models were validated with Monte Carlo calculations, and a qualitative comparison of dual-energy angiography with DSA showed similar image quality. While the energy-based methods are not necessarily optimized and further improvements are likely, it is concluded that both dual-energy and photon-counting approaches have the potential to provide similar iodine SNR to DSA for the same x-ray exposure.

ACKNOWLEDGMENTS

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APPENDIX A: LINEARIZATION OF THE LOG SIGNALS

We let \( A_0 = [A_{1b}, \ldots, A_{nb}] \) represent the point about which we expand the log signal \( \tilde{l} \) and \( \tilde{l}_0 \) be the corresponding log signal. Then

\[
\mathbb{E}\{\tilde{l} - \tilde{l}_0\} = -\mathbb{E}\left\{ \ln \frac{\hat{M}_i}{\hat{M}_i|A=A_0} \right\}.
\]

(A1)

Following the method of Cardinal and Fenster,\(^{40}\) we linearize the right side of the above equation about \( \hat{M}_i/\hat{M}_i|A=A_0 = 1 \)

\[
\mathbb{E}\{\tilde{l} - \tilde{l}_0\} \approx 1 - \mathbb{E}\left\{ \frac{\hat{M}_i}{\hat{M}_i|A=A_0} \right\}.
\]

(A2)

The quantity \( \hat{M}_i|A=A_0 \) would be determined from an average of a series of calibration scans, and we assume has negligible variability, therefore

\[
\mathbb{E}\{\tilde{l} - \tilde{l}_0\} \approx 1 - \int_0^\infty \frac{S_i(E)\hat{q}_i(E)e^{-\hat{A}_0(E)\gamma}}{S_i(E)\hat{q}_i(E)e^{-\hat{A}_0(E)\gamma}} dE.
\]

Linearizing \( \hat{M}_i \) about \( A = A_0 \) yields

\[
\mathbb{E}\{\tilde{l} - \tilde{l}_0\} \approx \sum_{b=1}^m \left( A_{ib} - A_{0b} \right) \frac{\mathbb{E}\{\tilde{l} - \tilde{l}_0\}}{\mathbb{E}\{\tilde{l} - \tilde{l}_0\}},
\]

where \( \frac{\mathbb{E}\{\tilde{l} - \tilde{l}_0\}}{\mathbb{E}\{\tilde{l} - \tilde{l}_0\}} \) denotes the average value of the mass-attenuation coefficient of basis material \( b \) weighted by \( S_i(E)\hat{q}_i(E)e^{-\hat{A}_0(E)\gamma} \).

In matrix notation, the above expression can be written as

\[
\mathbf{L} - \mathbf{L}_0 = \mathbf{J}(\mathbf{A} - \mathbf{A}_0).
\]

(A3)

APPENDIX B: LOG-SIGNAL COVARIANCE

In general, the covariance between log signals \( i \) and \( j \), Cov\{\( \tilde{l}_i, \tilde{l}_j \)\}, is given by

\[
\text{Cov}\{\tilde{l}_i, \tilde{l}_j\} = \mathbb{E}\{\Delta l_i \Delta l_j\},
\]

(A4)

where \( \Delta l_i = \tilde{l}_i - \mathbb{E}\{\tilde{l}_i\} \). A first order Taylor expansion of \( \tilde{l}_i \) about \( \mathbb{E}\{\hat{M}_i\} \) gives

\[
\tilde{l}_i \approx \tilde{l}_i|\hat{M}_i=\mathbb{E}\{\hat{M}_i\} + \left( \mathbb{E}\{\hat{M}_i\} - \mathbb{E}\{\hat{M}_i\} \right) \frac{\partial \tilde{l}_i}{\partial \hat{M}_i|\hat{M}_i=\mathbb{E}\{\hat{M}_i\}},
\]

(A5)

\[
\approx \mathbb{E}\{\tilde{l}_i\} - \mathbb{E}\{\hat{M}_i\} \frac{\partial \tilde{l}_i}{\partial \hat{M}_i|\hat{M}_i=\mathbb{E}\{\hat{M}_i\}},
\]

(A6)

\[
\Delta l_i = -\frac{\partial \tilde{l}_i}{\partial \hat{M}_i|\hat{M}_i=\mathbb{E}\{\hat{M}_i\}},
\]

(A7)

where \( \Delta \hat{M}_i = \hat{M}_i - \mathbb{E}\{\hat{M}_i\} \). Combining Eqs. (A4) and (A7)
\[
\text{Cov}\{\hat{I}_m, \hat{I}_j\} = \mathbb{E}\left\{ \frac{\Delta M_i}{\text{E}(M)} \frac{\Delta M_j}{\text{E}(M)} \right\} - \text{Cov}\{M_i, M_j\} \text{E}(M), \quad (A8)
\]

where \(\text{Cov}\{M_i, M_j\}\) is the covariance between \(M_i\) and \(M_j\). The exact form of \(\text{Cov}\{M_i, M_j\}\) depends on the specific imaging application.

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65E. S. Tanguay, Kim, and Cunningham: Theoretical comparison of energy-dependent and conventional subtraction angiography