Machine Learning-based Techniques to Address Spectral Distortions in Photon Counting X-ray Computed Tomography

by

MengHeng Touch

Graduate Program in Medical Physics
Duke University

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Joseph Y. Lo

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Robert E. Reiman Jr.

Thesis submitted in partial fulfillment of the requirements for the degree of Master of Science in the Graduate Program in Medical Physics in the Graduate School of Duke University 2016
Abstract

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Spectral CT using a photon counting x-ray detector (PCXD) shows great potential for measuring material composition based on energy dependent x-ray attenuation. Spectral CT is especially suited for imaging with K-edge contrast agents to address the otherwise limited contrast in soft tissues. We have developed a micro-CT system based on a PCXD. This system enables full spectrum CT in which the energy thresholds of the PCXD are swept to sample the full energy spectrum for each detector element and projection angle. Measurements provided by the PCXD, however, are distorted due to undesirable physical effects in the detector and are very noisy due to photon starvation. In this work, we proposed two methods based on machine learning to address the spectral distortion issue and to improve the material decomposition. This first approach is to model distortions using an artificial neural network (ANN) and compensate for the distortion in a statistical reconstruction. The second approach is to directly correct for the distortion in the projections. Both technique can be done as a calibration process where the neural network can be trained using 3D printed phantoms data to learn the distortion model or the correction model of the spectral distortion. This replaces the need for synchrotron measurements required in conventional technique to derive the distortion model parametrically which could be costly and time consuming. The results demonstrate experimental feasibility and potential advantages of ANN-based distortion modeling and correction for more accurate K-edge imaging with a PCXD. Given the computational efficiency with which
the ANN can be applied to projection data, the proposed scheme can be readily integrated into existing CT reconstruction pipelines.
To my beloved parents for the unconditional support and my advisor for the unwavering guidance and encouragement.
Contents

Abstract iv
List of Tables ix
List of Figures x
List of Abbreviations and Symbols xii
Acknowledgements xiv

1 Introduction 1
  1.1 Background ................................................. 1
  1.2 Spectral CT ............................................... 4
  1.3 Photon Counting X-ray Detectors ............................ 5
  1.4 3D printing ............................................... 7
  1.5 Artificial Neural Network .................................. 9

2 PCXD Spectral Response Modeling 11
  2.1 PCXD Distortion Model ................................. 11

3 Distortion Compensation in Spectral CT 15
  3.1 Statistical Projection Decomposition ....................... 15
  3.2 Projection Decomposition Using Parametric Distortion Model 17
     3.2.1 Simulation ........................................... 17
  3.3 Projection Decomposition Using ANN Distortion Model .... 21
     3.3.1 Artificial Neural Networks ......................... 22
3.3.2 Simulation ......................................................... 23

4 Distortion Correction for Spectral CT ........................................... 25
   4.1 Full-spectrum micro-CT ................................................. 25
   4.2 ANN Distortion Correction ............................................. 26
   4.3 Image-based Material Decomposition ................................. 30
   4.4 Simulation ............................................................... 31
      4.4.1 Method .............................................................. 31
      4.4.2 Result .............................................................. 32
   4.5 Phantom Data ............................................................. 33
      4.5.1 Method .............................................................. 33
      4.5.2 Result .............................................................. 35
   4.6 Ex-vivo Mouse Data ...................................................... 38
      4.6.1 Method .............................................................. 38
      4.6.2 Result .............................................................. 39

5 Conclusions ................................................................. 43

Bibliography .................................................................. 47
List of Tables

2.1 PCXD distortion model parameters. . . . . . . . . . . . . . . . . . . . 13
# List of Figures

1.1 Various charge interactions inside PCXD pixel ........................................ 7
1.2 A representation of a basis artificial neural network architecture. ....... 10
2.1 PCXD Distortion Model. ........................................................................... 14
3.1 Sinograms and FBP reconstructed images of the output material basis from the MLEM material decomposition. ................................. 19
3.2 Sinograms and FBP reconstructed images of the output material basis from the MLEM material decomposition using *imperfect* distortion model. ................................................................. 20
3.3 Flowchart of distortion compensation method using the ANN-based distortion model: (a) distortion model training and (b) its application in MLEM-based projection decomposition. ......................... 22
3.4 Sinograms and FBP reconstructed images of the output material basis from the MLEM material decomposition using ANN-based distortion model. ................................................................. 24
4.1 Full-spectrum CT projections data and reconstructed images of a physical 3D-printed phantom acquired with PCXD. ............................... 27
4.2 ANN Distortion Correction Flowchart. ...................................................... 28
4.3 Simulated, Digital and 3D Printed Phantoms. ........................................... 29
4.4 Spectral basis functions including the photoelectric effect (PE), Compton scattering (CS), and iodine. The PE and CS functions are scaled to sum to the attenuation of water. ........................................ 31
4.5 Comparison of spectral images before and after applying ANN distortion correction showing recovery of the iodine K-edge at 34 keV with the correction. ......................................................... 33
4.6  The decomposed material images using Compton scattering (CS) and photoelectric (PE) physical basis functions (normalized to water) and iodine from uncorrected and ANN distortion corrected spectral images. ........................................ 34

4.7  CNR plots evaluated for each vial in the simulated iodine phantom. 35

4.8  Comparison of corrected and uncorrected spectral CT images of a 3D printed phantom. ................................. 36

4.9  Phantom Data: Measured Attenuation .......................... 37

4.10 Phantom Data: Measured Enhancement (HU/(mg/ml)) .... 38

4.11 Phantom Data: Material Decomposition ....................... 39

4.12 Phantom Data: Measured Iodine Concentration ............. 40

4.13 Mouse Data: Distortion Correction ............................ 41

4.14 Mouse Data: Material Decomposition ....................... 42
List of Abbreviations and Symbols

Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>3D</td>
<td>Three spatial dimension</td>
</tr>
<tr>
<td>ANN</td>
<td>Artificial Neural Network</td>
</tr>
<tr>
<td>BF</td>
<td>Bilateral filtration</td>
</tr>
<tr>
<td>bfgs</td>
<td>Broyden-Fletcher-Goldfarb-Shanno</td>
</tr>
<tr>
<td>CNR</td>
<td>Contrast-to-noise ratio</td>
</tr>
<tr>
<td>CS</td>
<td>Compton scattering</td>
</tr>
<tr>
<td>CT</td>
<td>Computed tomography</td>
</tr>
<tr>
<td>CdTe</td>
<td>Cadmium telluride</td>
</tr>
<tr>
<td>CZT</td>
<td>Cadmium zinc telluride</td>
</tr>
<tr>
<td>DECT</td>
<td>Dual energy computed tomography</td>
</tr>
<tr>
<td>DRF</td>
<td>Detector response function</td>
</tr>
<tr>
<td>EID</td>
<td>Energy integrating detector</td>
</tr>
<tr>
<td>FBP</td>
<td>Filtered back-projection</td>
</tr>
<tr>
<td>FWHM</td>
<td>Full-width half maximum</td>
</tr>
<tr>
<td>HU</td>
<td>Hounsfield units</td>
</tr>
<tr>
<td>MLEM</td>
<td>Maximum likelihood expectation maximization</td>
</tr>
<tr>
<td>NIST</td>
<td>National Institute of Standards and Technology</td>
</tr>
<tr>
<td>PE</td>
<td>Photoelectric</td>
</tr>
<tr>
<td>PCXD</td>
<td>Photon counting x-ray detector</td>
</tr>
<tr>
<td>Acronym</td>
<td>Description</td>
</tr>
<tr>
<td>---------</td>
<td>---------------------------</td>
</tr>
<tr>
<td>PLA</td>
<td>Polylactic acid</td>
</tr>
<tr>
<td>PMMA</td>
<td>Polymethyl methacrylate</td>
</tr>
<tr>
<td>RMSE</td>
<td>Root-mean-square error</td>
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</table>
Acknowledgements

All work was performed at the Duke Center for In Vivo Microscopy, an NIH/NIBIB national Biomedical Technology Resource Center (P41 EB015897), with additional funding from the National Cancer Institute (R01 CA196667). The author would like acknowledge Devin Miles and the Duke Innovation Studio for assistance with 3D printing the phantoms. Lastly, I would like to acknowledge all members of the Center for In Vivo Microscopy for all the intellectual discussion and kind support in all aspects to make this work possible.
Introduction

1.1 Background

Computed tomography (CT) has been the dominant modality for imaging in both clinical and pre-clinical applications due to its very high spatial and temporal resolution. Conventional CT utilizes an energy integrating detector (EID), which measures the integrated signal produced by a polychromatic x-ray spectrum. Reconstruction yields an energy weighted image of linear attenuation coefficients at the effective energy. This loss of energy information results in some major limitations to current CT technologies, including poor soft tissue contrast and reduced accuracy of mass attenuation measurements [1].

To increase material discrimination, extra information on tissue composition can be provided via spectral CT by measuring the material-dependent attenuation of x-ray photons at different energies. Conventional spectral-CT was done in the form of dual-energy CT (DECT) where the subjects was scanned with two x-ray spectra to provide using EID, enabling a two-materials decomposition using the differential contrast in attenuation coefficient at the two tube voltages. However, the minimal
spectral contrast caused by overlapping spectra and the use of EID and the increase in dose are the limitations in adapting this method into higher spectral dimension to provide more accurate and true physical basis material decomposition.

Advancements in detector technology, specifically in photon counting x-ray detectors (PCXD) [2, 3], can mitigate the above mentioned limitations. PCXD have already shown great promise for increasing performance in quantitative material decomposition in spectral CT [1]. These detectors bin incoming photons based on their energy, acquiring detailed spectral information and potentially enabling the decomposition of several K-edge materials from a single scan. The spectral measurements are typically used for decomposition into physical or material basis functions, as described in [4], but show limited accuracy due to two majors issues: (i) the projection data is typically affected by spectral distortions due to physical effects in the detector such as charge sharing, K-escape energy loss, and pulse pileup [1, 3]; and (ii) the projection data is generally very noisy due to low photon counts at high and low energies relative to the source spectrum. 

Consequently, the primary objectives of this work are to develop and demonstrate a novel set of machine learning-based techniques to address spectral distortion in photon-starved, full-spectrum PCXD data to improve material decomposition performance.

Various empirical methods have been proposed to compensate for PCXD spectral distortions [5, 6]. Correction methods undo the distortion process, while compensation is used to offset the effect. The correction approach is ill-posed, because the number of energy bins for the available PCXDs is typically between two and eight and is much smaller than the number of parameters to fully describe the spectrum [7]. To work well, some assumptions about the material composition are used as constraints, e.g., the object consists only of water. The compensation approach of PCXD degradation factors can be achieved by incorporating a PCXD model as part of the
forward imaging process, and iteratively estimating either the imaged object or the line integrals using a maximum likelihood approach [6]. However, these techniques generally require a very accurate spectral distortion model of the PCXD derived usually from monochromatic synchrotron measurements [6] or interpolation of radioisotope measurements [8]. Other compensation methods to account for PCXD distortion include a lookup table approach [9] and approaches using ANN [5, 10] as an estimator to obtain material composition directly from distorted spectra. These approaches do not directly correct for the spectral distortion but they act as multidimensional estimators to map the distorted spectrum from a set number of energy bins to a set of known material basis functions. K-edge material was not included or discussed in these previous studies.

Due to the highly noisy nature of PCXD data, the ability to reduce noise is of exceptional importance for improving material detectability. In the case of K-edge material imaging [11], special attention is required when performing noise reduction in order to preserve the K-edge contrast. In ref. [12], a penalized weighted least squares approach was used to reduce noise and to produce reconstruction results consistent with the expected attenuation curves of the present materials (iodine, PLA, water, and gold). In this thesis, I employed a much more general post-reconstruction denoising scheme for spectral CT data that can be applied regardless of material composition, spectral distortions, and differences in noise level between energy bins, making it largely system and application independent. This approach is an extension of our previously published denoising scheme based on joint bilateral filtration with additional provisions to preserve K-edge contrast while enforcing spectral continuity developed by Clark et al. [13, 14].

In this work, we propose two novel ANN-based approaches to address the spectral distortion issue in pcxd-based spectral CT. The first approach uses an ANN to model the spectral distortion which was used as a distortion compensation in a statistical
projection decomposition technique, first proposed by Schlomka et al. [6]. The second technique is a direct distortion correction method where an ANN was trained to learn to undo the spectral distortion in projections data, which can be applied prior to image reconstruction and image-based decomposition.

1.2 Spectral CT

The idea of using spectral CT to obtain material composition information was first proposed by Alvarez and Macovski in 1975 as an energy selective reconstruction method for X-ray CT[4]. The proposed theory relied on the ability to acquire spectral information of the x-ray beam in addition to the beam intensity. The simplest implementation of spectral CT, DECT, scans the same subject with two different x-ray spectra, allowing separation of two materials. Previous works in our group have demonstrated preclinical, functional imaging applications of EID-based DE micro-CT involving the separation of iodine and calcium or iodine and gold, including classification of atherosclerotic plaque composition [15], non-invasive measurement of lung [16] and myocardial perfusion [17], and the classification of tumor aggressiveness and therapy response in the lungs [18] and in primary sarcoma tumors [19, 20]. Several factors limit further development and adoption of DE-CT imaging protocols. Chief among these is the relative insensitivity of polychromatic x-ray spectra to energy-localized, material-specific changes in x-ray attenuation (e.g. K-edges). This spectral insensitivity is caused by the lack of energy resolving power associated with EIDs. In addition, to enable true physical basis material decomposition as proposed in [4], a set of more than two energy bins of the spectra is required.

This limitation was overcome with the introduction of energy sensitive photon counting x-ray detector which could enable acquisition of up to 8 energy bins in one scan (see Chapter 1.3). This development has allowed great potential of spectral CT in not only reducing dose in CT but also in becoming a functional imaging modal-
ity. In PCXD-based spectral CT, each projection is acquired in multiple energy bins in a single exposure and the images in each bin are then reconstructed providing another dimension of image contrast along the energy domain called spectral contrast. Various studies have shown many potential applications of spectral CT such as improving contrast to noise ratio (CNR) [21–24], reducing dose [1], reducing beam hardening artifacts [1], quantitative K-edge imaging [4, 22], simultaneous multi-contrast agent imaging [6, 14] and enabling molecular CT for personalized medicine using nanoparticle contrast agents [14, 25–29].

In this work, we will focus mainly in K-edge imaging, specifically iodine nanoparticle, and the ability to not only identify K-edge material but also accurately quantify its concentration. The energy thresholds of each energy bin can be defined to fit specific application which provide the flexibility to optimize for imaging of K-edge materials. The ability to sample more than 2 energy bins also allows us to perform material decomposition into true physical basis (ie. Compton’s scattering and photoelectric) and any additional K-edge material basis (see Chapter 4.3).

1.3 Photon Counting X-ray Detectors

As mentioned above, the current advancement in PCXD has brought forth many possibilities in extending CT imaging into the functional domain. However, the current performance of PCXD is still far from being perfect [1]. One of the main flaws in current PCXD systems is the low spectral fidelity due the physical effects in the solid state detector. Typical materials for PCXD are solidstate compounds such as cadmium telluride (CdTe), cadmium zinc telluride (CZT) or silicon (Si) which was chosen for it effective absorption of X-ray photons in the diagnostic range (1-140 keV). However, the spectral measurement in PCXD may not reflect the true spectral distribution of the incident spectra due to the following physical effects:
• **Charge sharing:** The charge collection mechanism in the detector relies on the application of high voltage bias. The electric field generated by the bias voltage drives the charges created by the photon interactions in the detector material to be collected by an electrode for the specific pixel. However, if the charge cloud, created by the photon absorption in the detector, occurs close to the boundary between pixels, more than one neighboring pixel would falsely register the count at energies lower than the incident photon energy (see Fig. 1.1(a)).

• **K-escape energy loss:** In the event that photons interact with the detector material through photoelectric effect, a K-shell electron from the atom is released which is then filled by an inner shell electron. This process causes an emission at the transition energy which might be detected by the same pixel (see Fig. 1.1(b)), a neighboring pixel (see Fig. 1.1(c)) or leave the detector completely. In these events, the signal registered count by the pixel is an energy lower than the true photon energy by the K-shell energy of the material. In the case that the lower energy K-escape photon does not leave the detector, it could be detected again by the same pixel as a separate event or pileup event or by a neighboring pixel at the emitted K-shell energy.

• **Pulse pileup:** This effect occurs when the photon count rate is higher than the detector ability to resolve the event in time. The severity of the effect depends on the incident counts rate and detector deadtime. The effect of the overlapping pulses causes the PCXD to record events at energies higher than the true incident photon energies which results in spectral distortion in the overall detector response.

• **Compton scattering:** Instead of being absorbed immediately when entering the PCXD material, the photon can be scattered off the material and loses some
Figure 1.1: Various interactions between incident x-ray photons and PCXD pixels [1]. (a) shows charge sharing effect caused by interaction near the boundary between two adjacent pixels. (b) shows K-escape mechanism where a photon imparts the PCXD material and loses some energy equivalent to K shell emission energy of the material. In this case, the K-escape photon was absorbed by the same pixel. (c) shows another K-escape event but the escaped photon is absorbed by a neighboring pixel. (d) shows multi Compton scattering events and part of the charge cloud might be absorbed by the adjacent pixel. All results in lower energy detected.

of its energy in the process. After the initial Compton scattering event, the lower energy photon may change direction and it may be absorbed by the same pixel, a neighboring pixel or leave the detector completely. The Compton scattering interaction loss is a continuous function so the result of this effect is a continuous lower energy background tail in the detector response (see Fig. 1.1(d)).

1.4 3D printing

A big part of our method relies on the ability to accurately fabricate a calibration phantom from a digital 3D model. This is made possible with 3D printing technology which has recently gained much traction in the biomedical domain. 3D printing
technology has been widely used as a prototyping tool in many industries and it works by layering material to create a 3D object layer by layer from a digital model. Although most printer follows the same technique of the layering the material, different mechanism was used to fused the material together which could have an effect on print resolution, speed and the ability to print multiple material. Currently, there are 4 main technologies used in various grades of 3D printer:

- **Fused deposition modeling (FDM):** The printing material (usually thermoplastic such as polylactic acid (PLA) and Acrylonitrile butadiene styrene (ABS)) are fed into the printer and guided into a heated nozzle. The heated nozzle melts the material and extrude out the melted plastic layer by layer to create the shape of the 3D object. [30] This is currently one of the most popular technologies used in 3D printing currently due to its relatively simple technology and very low cost to build.

- **Selective Laser Sintering:** This techniques uses a laster to melt material powder layer by layer to construct the 3D objection. This process is mainly used in industrial 3D printer for its precision and bigger selection of material choice.

- **Powder bed and binder:** This technique also uses powder material but instead of laser it uses an inkjet head to inject the binder material on the powder bed. This technique has the advantage of printing in multiple color.

- **Stereolithography (SL):** this is a more recent technology using ultraviolet laser to slowly harden resin liquid material layer by layer. This technique also has the advantage of the ability to print at very high resolution at the cost of the relative expensive resin material.
In our study, we tested printing the phantom using both the FDM and the SL technologies on Makerbot 2 and Formlabs printers respectively. The FDM method was chosen at the end for its known material composition and the lower attenuation coefficient of the material which is very close to that of water.

1.5 Artificial Neural Network

The invention of artificial neural network (ANN) was inspired by the biological network in human brain [31, 32]. One of the earliest example of an ANN was a simple single layer perceptron with an input and output layer by Rosenblatt in the 1950s [33]. However, this early perceptron model can only represent linear function. From the 1960s to the 1980s, further development in the field of artificial intelligence has led to the introduction of non-linear hidden layer and back-propagation training algorithm which was thought to have enabled the use of ANNs to compute any functions [34, 35]. For its ability to learn and model highly non-linear function, ANNs has gain enormous popularity in the artificial intelligence community and its application in computer vision started to flourish ever since. With the work of many pioneers in the field of artificial intelligence such as Geoff Hinton, Yann LeCun and Yoshua Bengio, the application of artificial neural networks has reached one of its peaks in computer vision where a deep learning algorithm called convolutional neural network was used by Hinton et al [36] to achieve extraordinary performance in image recognition in the ImageNet challenge in 2012. In our work, instead of the classic image recognition application of ANNs in computer vision, we employed an ANN to model the highly non-linear distortion in the PCXD response (Chapter 3) or a distortion correction by training it in reverse (Chapter 4).

The basic architecture of an ANN consists of an input layer, an output layer and a number of hidden layers defined by the user (see Fig. 1.2). Each layer is composed of various numbers of neurons which can also be called nodes. The complexity of the
Figure 1.2: A basic ANN architecture. (a) shows the general structure of a ANN consisting of an input layer, a hidden layer and an output layer. The number of hidden layer can be increase based on the complexity of the function to model. (b) shows a representation of the computation that takes place at each nodes which consist of a weighted sum operation including a bias term and parsing the sum into an activation function to compute the output value of the node.

ANN is defined by the the complexity and the number of hidden layers and neurons in each layer. The numbers of neurons of input and output layers are defined by the dimensions of the input and target data set to be modeled, respectively. The inner layers or hidden layers can be configured by the users to have the number of neurons to fit with the complexity of the problem. The more neurons in each layer and the more layers in the network, the more complex the ability of the ANN to model will be. However, the complexity of the network comes with the price of computation time, especially during the training process, and the likelihood of over-fitting. The ANN architecture has to be selected to fit the scale of the problem in question to balance the bias and variance associating with the quality of the ANN training. There are many factors that play roles in the bias and variance of an ANN including the quality and size of the training data set and the complexity of the network.
2.1 PCXD Distortion Model

A limitation of PCXD-based imaging using CdTe can be the degradation of the energy response due to physical effects like charge sharing between detector elements, pulse pileup, and energy loss due to K-escape [1]. This energy response degradation causes a distortion in the measured energy spectrum which deviates from the incoming x-ray spectrum. To compensate for this distortion, a detector response function (DRF) was experimentally determined following the model first described in [6]. The DRF model includes two Gaussian peaks: one at the incident photons energy and one at the K-escape energy of CdTe. An additional background term models a lower-energy tail. Hence, the DRF, \( R(U,E) \), at energy \( U \) resulting from incident photons of energy \( E \) interacting with the detector can be modeled as:

\[
R(U,E) = c_1(E) \left[ \frac{1}{\sqrt{2\pi}\sigma_1(E)} e^{-\frac{(U-E)^2}{2\sigma_1(E)^2}} + \frac{c_2(E)}{\sqrt{2\pi}\sigma_2(E)} e^{-\frac{(U-E_\text{e}-E)^2}{2\sigma_2(E)^2}} + B(U,E) \right] \tag{2.1}
\]

where \( \sigma_1 \) and \( \sigma_2 \) represent the energy spread of the incident photon peak and the K-escape peak, respectively. \( E_\text{e} \) is the average escape photon energy of the detector
material (∼ 25 keV for CdTe). The background term, \( B(U, E) \), depends on both the measured and incident photon energy. \( B(U, E) \) is modeled as the product of the measured energy, \( U \), and a constant \( c_3(E) \) for \( U < E - 3\sigma_1 \) and linearly decreases to zero over the range \( U = E - 3\sigma_1 \) to \( U = E + 3\sigma_1 \). The constant \( c_1(E) \) is a scaling factor such that the number of incoming photons is conserved. The width of the photo peak and K-escape peak are assumed to be the same (i.e. \( \sigma = \sigma_1 = \sigma_2 \)). The constant terms \( c_2(E), c_3(E), \) and \( \sigma(E) \) are further parameterized as follows:

\[
C_2(E) = \begin{cases} 
 a_1 e^{-a_2 E} & \text{for } E > E_e \\
 0 & \text{otherwise}, 
\end{cases} 
\]

\[C_3(E) = a_2 - a_4 E\]  \hspace{1cm} (2.2a)

\[\sigma_1(E) = \sigma_2(E) = \sigma(E) = a_5 + a_6 E\]  \hspace{1cm} (2.2b)

The parameters in Equation (2.2) were derived based on the values given in [6] and based on experimental data acquired from 109Cd and 133Ba radioactive sources measured by our PCXD, and then compared with the expected spectra for these isotopes given 1-keV sampling. The sources were placed ∼ 5 cm in front of the PCXD during sampling. A full-spectrum acquisition with an integration time of 5 seconds for each energy was performed for each of the two sources. The pixels were averaged to provide a one-dimensional signal of number of counts over the energy spectrum. The spectral data was next read into MATLAB (MathWorks, Natick, MA) and used for fitting the DRF model. The term \( c_2(E) \), containing parameters \( a_1 \) and \( a_2 \), was chosen to be the same as the value given in [6]. The rest of the parameters were derived by fitting the DRF model to the measurements by selecting values which minimized the root mean square error (RMSE) of the fit. For the 109Cd source spectrum, a photo peak at 22 keV was modeled. For the 133Ba source, three peaks at 31 keV, 35 keV, and 81 keV were modeled and scaled by their respective branching ratios (LBNL Isotopes Project, http://ie.lbl.gov/toi/; LNHB Table of Radionuclides,
Table 2.1: Resulting parameter values obtained from [6] and Equations (2.1) and (2.2) after fitting the expected and detected spectra for 109Cd and 133Ba.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Value</th>
</tr>
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<tr>
<td>$a_1$</td>
<td>0.5</td>
</tr>
<tr>
<td>$a_2$</td>
<td>$0.015keV^{-1}$</td>
</tr>
<tr>
<td>$a_3$</td>
<td>$0.003keV^{-1}$</td>
</tr>
<tr>
<td>$a_4$</td>
<td>$0.300 \times 10^{-4}keV^{-2}$</td>
</tr>
<tr>
<td>$a_5$</td>
<td>$1.16keV$</td>
</tr>
<tr>
<td>$a_6$</td>
<td>0.025</td>
</tr>
</tbody>
</table>


The results of spectral distortion modeling are presented in Fig. 2.1 and Table 2.1. Fig. 2.1(A) and 2.1(B) compare the model fitted and experimentally measured spectra for 109Cd and 133Ba, respectively. The measured spectral peaks appear to be accurately positioned using our CdTe-based PCXD. The full width half maxima (FWHM) for the most significant peaks were 2.9 keV for 109Cd (at 22 keV) and 3.2 keV for 133Ba (at 31 keV). Fig. 2.1(C) shows the undistorted, 70 kVp, polychromatic tungsten spectrum (0.7 mm Al filtration, provided by Spektr [37]) and the corresponding modeled distorted x-ray spectrum along with the measured x-ray spectrum in air (no object between the x-ray source and the detector) using our PCXD. The distortion model applied to the simulated 70 kVp x-ray spectrum very closely matched the measured spectrum. For a quantitative comparison, we also computed the root mean square error (RMSE) between the measured and modeled spectra from 10 to 120 keV to quantify the accuracy of the model. The resulting RMSE values were 0.0111, 0.0069 and 0.0016, respectively, for 109Cd, 133Ba, and the 70kVp polychromatic spectrum. Finally, Fig. 2.1(D) displays the DRF as a matrix in which we note the low-energy tailing effect and the K-edge escape peak from CdTe for incident photons with an energy higher than 25 keV.
Figure 2.1: Distortion modeling. In (A) and (B) we plot the fitting model and the corresponding measured spectra for Cd-109 and Ba-133, respectively. Plot (C) shows the expected, undistorted 70 kVp polychromatic spectrum (red), as well as the same spectrum after applying the spectral distortion model (solid, blue line). A corresponding measured spectrum acquired with our PCXD at 70 kVp is also shown (blue circles). The 2D display in (D) represents the DRF, showing the low energy tailing effect (black arrow) and the K-edge escape peak for CdTe for incident photons with energy higher than 25 keV (white arrow).
Distortion Compensation in Spectral CT

One possible way to account for PXCD spectral distortion is to use model-based statistical reconstruction which allows for the distortion compensation by including a distortion in the forward statistical model. A projection decomposition technique was implemented to perform maximum likelihood expectation maximization (MLEM) based material basis estimation of the line integrals. Two simulation experiments were performed to study this technique in compensating for spectral distortion using two different distortion models. The first simulation used the parametric detector response function models derived via the radioisotope measurements (see Chapter 2) whereas the second simulation used the ANN-based distortion model (see Section 3.3). Both the parametric and ANN distortion models provide a full-spectrum distortion transformation (21-60 keV range of interest for ANN case), which allows the flexibility of any binning configuration in the forward model.

3.1 Statistical Projection Decomposition

As proposed by Schomka et al. in [6], a maximum likelihood expectation maximization (MLEM) based method can be used to estimate the material composition in
the projection domain. This technique requires a full forward model of the imaging chain, including the source spectra, object attenuations, and the detector response function. The inclusion of the detector response allows us to take into account the physical effects associated with the detector and to compensate for the resulting distortion in its spectral response. As fully derived in [6], Equation (3.1) describes the expected value $\lambda_i$, of the number of photons in energy bin $i$:

$$
\lambda_i(A_\alpha) = \int_0^\infty S_i(E)\Phi(E) \exp \left( - \sum_{\alpha=1}^{n_{\text{bin}}} f_\alpha(E) A_\alpha \right) D(E) dE, \quad i = 1, 2, \ldots, n_{\text{bin}} \quad (3.1a)
$$

$$
A_\alpha = \int a_\alpha(\vec{x}) ds, \quad a = 1, \ldots, n_{\text{mat}} \quad (3.1b)
$$

where $\Phi(E)$ models the source x-ray photon fluence, $D(E)$ denotes the detector absorption efficiency, $f_\alpha(E)$ refers to the material basis, and $a_\alpha(\vec{x})$ denotes the density coefficient of the material $a$ to be solved for the number of materials ($n_{\text{mat}}$) in the decomposition basis. $S_i(E)$ was originally described as a bin sensitivity function and $R(E, U)$ as the detector response function derived from fitting monochromatic synchrotron measurements of the spectral distortion:

$$
S_i(E) = \int_{U_i^-}^{U_i^+} R(E, U) dU, \quad i = 1, 2, \ldots, n_{\text{bin}} \quad (3.2)
$$

where $U_i^-$ refers to the $i$th energy threshold. For the purpose of this study, the detector response function was obtained for our CdTe-based PCXD using two different techniques: 1) by fitting a physical model proposed in [6] using radioisotopes measurements as described by us in [14], and 2) using an ANN to learn the distortion model, as detailed in the next sections.

Given that the number of energy bins is typically equal to or greater than the number of materials to be estimated, a maximum likelihood approach is used to
perform the parameter estimation in this overdetermined problem. By modeling the projection measurements \( (m_i) \) as independent Poisson random variables, the likelihood function can be calculated as follows:

\[
P(m_1, \ldots, m_{nbin}|\lambda_1(A_\alpha), \ldots, \lambda_{nbin}(A_\alpha)) = \prod_{i=1}^{nbin} \frac{\lambda_i(A_\alpha)^{m_i}}{m_i} e^{-\lambda_i(A_\alpha)}
\] (3.3)

The basis function coefficients were estimated by minimizing \( L \), the negative log of the likelihood function \( P \):

\[
L(m_1, \ldots, m_{nbin}|A_\alpha) = -\ln [P(m_1, \ldots, m_{nbin}|\lambda_1(A_\alpha), \ldots, \lambda_{N}(A_\alpha))] = \sum_{i=1}^{N} [\lambda_i(A_\alpha) + \ln(m_i!) - m_i\ln\lambda_i(A_\alpha)]
\] (3.4)

Thus, the line integrals \( (A_\alpha) \) for each material basis were estimated with a non-linear optimizer, i.e the quasi-Newton nonlinear optimization algorithm of Broyden-Fletcher-Goldfarb-Shanno (bfgs) [38–41] implemented in MATLAB (MathWorks, Natick, MA). Material images were then reconstructed from the line integrals using filtered back projection (FBP) with a Ram-Lak frequency filter.

3.2 Projection Decomposition Using Parametric Distortion Model

3.2.1 Simulation

We performed realistic simulations using the Spektr package [37] to generate ideal spectral projection data for both training and testing. Our simulated acquisition used a 75 kVp source spectrum with an integrated flux of 50000 photons per pixel line integral for 90 projections acquired over 180°. The projections were simulated in full-spectrum mode with 1 keV energy sampling. The parametric spectral distortion model derived for our system, as described in Chapter 2, was applied to the ideal
projections to simulate a set of distorted projections as closely matched to our detector as possible. In all simulations, we studied the performance of each technique with and without noise. In the noisy case, Poisson noise was added to the full-spectrum projection data in all energy bins, which corresponded to a maximum reconstructed standard deviation of 230 HU of noise in the most photon-starved bins (~60 keV) and minimum of ~75 HU in the bin with the most photons (around the center part of the spectrum ~35-40 keV). The forward model was binned into 6 energy bins between 21, 27, 33, 38, 45, 51, and 60 keV, respectively, aiming to bracket the K-edge of iodine for maximum contrast.

Following reconstruction, the relative errors between mean iodine concentrations measured in each vial and the expected concentrations were computed, and the mean of this relative error over all vials was used to report the accuracy of iodine concentration estimation for each method. We also computed the root mean square error (RMSE) for comparison between the three techniques. Additionally, we computed the contrast-to-noise ratio (CNR):

\[
CNR = \frac{|m_1 - m_1|}{\sqrt{\sigma_1^2 + \sigma_2^2}}
\]

(3.5)

where \( m \) refers to mean values and to standard deviations computed in two adjacent regions of interest, 1 and 2. In the resulting images CNR was computed for the iodine relative to water. CNR was used to estimate the iodine detectability levels (Roses criterion: CNR = 5 [42]) and RMSE with respect to the reference phantom was evaluated and compared with and without distortion correction.

Two test cases were performed to study how sensitive this projection decomposition is to the accuracy of the distortion model. In the first case, we used the ground truth known distortion model as distortion compensation in the forward model, whereas in the second case a slightly inaccurate model was used.
Figure 3.1: Sinograms and FBP reconstructed images of the output material basis from the MLEM material decomposition. The simulation uses the perfect, known distortion model to compensate for the distortion in both cases: without noise (left) and with noise (right).

**Known Parametric Model**

Figure 3.1 shows the resulting material basis sinograms and reconstructed material decomposed images using the projection decomposition technique with the perfectly known physical distortion model to compensate for distortion. Without noise, the technique provides very high-quality material decomposition with a mean relative error in iodine concentration estimation of 7.78%. Iodine concentrations as low as 2 mg/ml can be detected (based on Roses criterion of $CNR \geq 5$ [42]). With noise, the result was degraded with the mean relative error increasing to 16.72%. Detectability was lost even for the most concentrated vial with 14 mg/ml of iodine.

**Inaccurate Parametric Model**

To provide a fair comparison to a real-case situation, in our first simulation, a projection decomposition with an imperfect physical distortion model was also simulated. The imperfection was introduced as a form of 10% degradation in full width at half
Figure 3.2: Sinograms and FBP reconstructed images of the output material basis from the MLEM material decomposition. The simulation includes an imperfection in the distortion model used to compensate for the distortion. Cases without noise (left) and with noise (right) are shown.

maximum (FWHM) of the Gaussian peaks and 10% underestimation of the background term in the model explained in Chapter 2. This degradation simulation was performed to provide insight on how sensitive the technique is to the accuracy of the parametric distortion model.

Figure 3.2 shows notable degradation in quality of the material decomposition with the imperfect distortion model, which contains 10% inaccuracy in the FWHM $\sigma(E)$ and the background constant term $B(U,E)$. This reduction in the ability of the projection decomposition to provide accurate material estimation is evident with an average of 49% underestimation of iodine concentration in the noiseless case and 50.22% underestimation with the presence of noise. The CNR follows the same trends where the noiseless results show detectability of 5 mg/ml iodine solution, but no vial could be claimed detectable under the presence of noise. Such results confirm the importance of a very accurate distortion model for distortion compensation using
projection decomposition techniques where a 10% imperfection can lead to tremendous degradation in both accuracy of the material estimation and its detectability.

3.3 Projection Decomposition Using ANN Distortion Model

To avoid the need for synchrotron and/or radioisotope measurements, we propose here a novel technique to derive the spectral distortion model using an ANN. The ANN has the ability to learn the highly nonlinear distortion model from a tomographic calibration scan, which makes the approach more accessible than the fitting of a parametric physical model. Our ANN training assumes the existence of a perfect set of projections, which can be obtained in practice by simulations and modeling using a digital phantom. Such a phantom could be 3D-printed and scanned to create expected projections for a calibration scan. The reconstructed CT phantom is next registered to its digital version to ensure that the two sets of projections are spatially matched. As a training phantom, we used a round phantom made with polylactic acid material (PLA), containing vials of 0 to 14 mg/ml of iodine in water. The selection of PLA was based on further studies using 3D printed PLA phantoms. Once the ANN training was completed, a different square phantom containing square vials of 0 to 14 mg/ml of iodine in water was used for testing.

Following the registration performed in MATLAB using correlation-based image registration function, we trained the ANN to learn the transformation from the distortion-free spectra to the distorted spectra (i.e. each projection pixel intensity across all energies at the same angle) in a calibration step (Fig. 3.3 (a)). Once the training was completed, the trained ANN could be used to perform distortion correction on any subsequent projection data acquired with the same CT system, acquisition parameters, and basis materials (Fig. 3.3 (b)).
3.3.1 Artificial Neural Networks

Similar to Zimmerman et al. [5], we used an ANN architecture composed of one input layer, two hidden layers, and one output layer. The input and output layers contained 40 nodes each, which correspond to 40 desired input and output energy bins (from 21 to 60 keV), respectively. Each hidden layer contained 5 neurons, each of which represents a sigmoid activation function. Each node in the output layer is modeled by a linear approximation function. In our simulation and experimental study, the ANN was trained using the Neural Network Toolbox in MATLAB. The ANN learning algorithm minimizes the mean square error between the estimated distorted spectra and the target spectra using the Levenberg-Marquardt back-propagation technique [43] implemented in MATLAB. During training, the weights of the neural network are calculated iteratively by optimizing the matching between the neural network output and the target spectrum via a minimization of the mean square errors. This
requires knowledge of the input ground-truth, distortion-free projections, which can be obtained by simulating the scan of digital phantoms using ideal x-ray spectra for the x-ray tube and CdTe-based detector absorption generated with Spektr [37].

3.3.2 Simulation

In our second simulation, we successfully integrated the ANN-based distortion model into the forward model of the projection decomposition technique and performed material decomposition on the same test phantom as the previous simulation. As shown in Figure 3.4, the resulting decomposed material sinograms and images are of at least comparable quality as the case where the distortion is perfectly known. In the noiseless simulation, the mean relative error in iodine concentration is 10.66%, and the lowest iodine concentration detectable by this technique is below our lowest simulated vial of 2 mg/ml (CNR=6.54). With noise added, the mean relative error is 11.82%, and the CNR follows the same trend as the previous method where no vial met the Roses criterion for detectability. In the presence of noise, the ANN model was able to work robustly and improved the accuracy of iodine concentration estimation by 5% over using the exact physical distortion model used to create the phantom in the first place.

Furthermore, it is evident that this technique of using a distortion model learned by an ANN in the forward model greatly outperforms the previous technique, where an imperfect model was used, and improves material decomposition. The distortion compensation technique using an ANN reduced the mean error in iodine estimation by 28% over using an imperfect model containing 10% degradation.
Figure 3.4: Sinograms and FBP reconstructed images of the output material basis from the MLEM material decomposition. The simulation used the ANN distortion model to compensate for the distortion and both cases without noise (left) and with noise (right) are shown. The ANN model was able to perform robustly even in the presence of noise.
Distortion Correction for Spectral CT

Another way to deal with PCXD spectral distortion is to directly correct for the distortion in the projection as pre-processing step. As mentioned in Chapter 1, this is a highly non-linear and ill-posed problem to which a direct inversion of the spectral distortion cannot be derived through some form of parametric model. To circumvent this problem, I propose an ANN-based distortion correction approach where the machine learning algorithm was used to learn the spectral correction to the distorted spectra in the projection data. In this chapter, I will detail the entire process of deriving the ANN distortion correction and applying it to correct for spectral distortion in data from a subsequent phantom and a rodent scan.

4.1 Full-spectrum micro-CT

We have developed a micro-CT system consisting of a CdTe-based PCXD (DxRay Inc., Northridge, CA), with 4 rows of 64 detector elements, each 1.0 mm x 1.4 mm in size and 1.0 mm thick. The PCXD can be operated in 4-energy-threshold mode or energy sweeping scan mode (also known as full spectrum mode). Full spectrum mode densely samples the entire energy spectrum. The system uses a polychromatic
x-ray tube (Varian G297) with a tungsten anode which produces an incoming beam which is attenuated with 5.6 cm of PMMA, 0.1 cm of Al, and 0.1 cm of Cu. We used this system for acquisitions in full spectrum CT mode at 75kVp with 0.6mA and 9.86-second exposures at each projection angle. Each exposure was used to sample all energies. 90 projections over a 180⁰ arc were acquired in full-spectrum mode. The energy threshold of the PCXD was swept in 1-keV increments, providing projection data in 120 energy bins. The source-to-detector distance is about 80 cm (mag.: ~1.1x), which allows us to use a parallel beam approximation for image reconstruction. We have imaged phantoms containing iodine solutions of different concentrations and water. The tomographic image sets were reconstructed using filtered back projection (FBP) with a Ram-Lak frequency filter at each energy bin. Two of the major limitations for spectral CT are the spectral distortions and the highly noisy nature of projections due to the limited photon counts in each bin. This results in very noisy reconstructed images (Fig. 4.1). The results are also affected by spectral distortions caused by the PCXD. The effects of spectral distortions are less obvious but can be observed by the lack of K-edge contrast enhancement in iodine between 33 and 34 keV.

4.2 ANN Distortion Correction

Although the PCXD provides full-spectrum x-ray projections, the energy distortion associated with the physical system heavily diminishes the signal from K-edge materials, and hence reduces the sensitivity of K-edge material decomposition. An ANN was used to reverse the distortion in the PCXD caused by the undesirable physical effects in the detector (detailed in Chapter 2). The motivation for using a neural network to perform the distortion correction is to exploit its ability to learn and model the highly non-linear relationship between the expected and the recorded spectral measurements, transforming the distorted projection data (input) to its correspond-
Figure 4.1: Full-spectrum CT data acquired for a physical 3D-printed phantom. (Left) System-calibrated and log-transformed sinograms from 21 keV to 60 keV acquired using a 75 kVp spectrum. (Right) FBP reconstructions of the sinogram data. Note the noise in the sinograms and reconstructions at the lowest and highest energies. The units of the calibration bars are in $cm^{-1}$.

The ANN-based approach we use for distortion correction is illustrated by the flowchart in Fig. 4.2 and contains both training and testing. We trained the ANN to learn the relationship between the distorted spectra (i.e. each projection pixel intensity across all energies at the same angle) and the expected, distortion-free spectra in a calibration step (Fig. 4.2 (a)). This training phase can be treated as a detector calibration process for a PCXD-based CT system which could be done on a phantom designed to match the attenuation ranges of that typically seen in the target applications. The current design of the phantom was done to match the attenuation range one could expect in a small animal scan and the same design can be easily adapted to human scanner by scaling the size of the phantom to match the range of a human cross-section. Once the training is completed, the trained ANN can be used to perform distortion correction on any subsequent projection data acquired with the same CT system, acquisition
Figure 4.2: A flowchart showing (a) neural network training as calibration process using a distorted tomographic projection scan of a calibration phantom and its synthesized, digital, ideal projection. (b) Application of the neural network to perform distortion correction before the images are reconstructed, filtered, and decomposed into basis materials.

parameters, and basis materials (Fig. 4.2 (b)). To mitigate the issue of very high noise level associated with spectral CT, we employed a post-reconstruction denoising scheme using joint bilateral filtration (BF), as detailed in [13, 14].

Assuming relatively similar level of complexity in correcting for the distortion as forward modeling the distortion (see Section 3.3), we used the same ANN architecture composed of one input layer, two hidden layers, and one output layer. The input and output layers contained 40 nodes each, which correspond to 40 desired input and output energy bins (from 21 to 60 keV), respectively. However, in this case the input and output training dataset was fed in reverse to the setup used to model the distortion. For the ANN to learn the correction to the distortion, the distorted spectra was used as input while the ground-truth, distortion-free, spectra was used as target in the training. In both our simulation and experimental

28
study, the ANN was trained using the Neural Network toolbox in MATLAB (MathWorks Inc., Natick, MA). The ANN learning algorithm minimizes the mean square error between the estimated distortion corrected spectra and the true target spectra using the Levenberg-Marquardt backpropagation technique [43] implemented in MATLAB. During training, the weights of the neural network are calculated iteratively by optimizing the matching between the neural network output and the target spectrum via a minimization of the mean square errors. This requires knowledge of the ground-truth, distortion-free projections which can be obtained by simulating the scan of digital versions of 3D printed phantoms (Fig. 4.3) using ideal X-ray spectra for the x-ray tube and CdTe based detector absorption generated with Spektr [37]. To ensure the input and target set match as closely as possible, we designed digital phantoms using Autodesk 3D modeling software. From the digital phantoms,
two physical phantoms were then 3D printed using polylactic acid (PLA) plastic material and a Makerbot Replicator 2 3D printer. The phantoms were 3D printed at 0.2 mm resolution which is sufficient to ensure a negligible difference between the digital version of the phantom and its 3D printed replica, given our PCXD pixel size of 1mm x 1.4mm.

4.3 Image-based Material Decomposition

One of the promises of full-spectrum CT is improved performance in material separation via material decomposition. To decompose spectral CT data containing a mixture of different materials into quantitative, 3D maps of the concentrations of each element, we focus here on a post-reconstruction decomposition method. Extending the approach of Alvarez and Macovski [4], we perform a basis material decomposition [22]:

\[ \mu(E) = \alpha_{PE}\mu_{PE}(E) + \alpha_{CS}\mu_{CS}(E) + \alpha_I\mu_I(E). \] (4.1)

For our implementation, the first two terms in eq. (4.1) describe the energy-dependent attenuation, \( \mu(E) \), in terms of photoelectric effect (PE) and Compton scattering (CS). These PE and CS components are scaled to sum to the attenuation of water when \( \alpha_{PE} = \alpha_{CS} = 1 \). The 3rd term is the attenuation of the K-edge material, iodine (Fig. 4.4). The material decomposition is performed with the system calibrated material sensitivity matrix \( M \) consisting of \( \alpha_{PE}, \alpha_{CS} \) and \( \alpha_I \). Our post-reconstruction material decomposition uses non-negativity constraint on the material concentrations, \( C \).

\[ M = [\alpha_{PE}, \alpha_{CS}, \alpha_I]; \]

\[ C = \arg\min_C \frac{1}{2}\|\mu - CM\|^2 \quad \text{subject to } C \geq 0. \] (4.2)

The optimization in equation (4.2), called subspace projection, reflects the physical reality that concentrations cannot be negative. In general, negative concentrations
4.4 Simulation

4.4.1 Method

We performed a realistic simulation using Spektr [37] to generate ideal projection spectra of a round phantom containing vials with 0 to 14 mg/ml of iodine in water, the typical concentrations that we encounter using an iodinated blood pool contrast agent in mouse studies [44]. The distortion, derived for our system using the spectral model (see Chapter 2), was introduced into the ideal sinograms to simulate a set of spectrally distorted projections as closely matched to our PCXD measurements as possible. Poisson noise was also added to match the levels of noise and the same number of photon counts in the real sinograms for each energy bin. The distorted and ideal spectral projections were then fed into our ANN training as
input and target, respectively to provide training. The training was done using 180 projections of a simulated tomographic calibration scan (90 raw, noisy projections and 90 re-projections of BF filtered [13, 14] reconstructions). The mixed use of noisy and denoised projections was preferred for training such that ANN could learn some denoising capabilities. Once the ANN training was completed, a different test phantom containing square vials with 0 to 14 mg/ml of iodine in water was simulated in a similar manner (see Fig. 4.3). The trained ANN was then applied to the distorted projections of the test phantom to obtain distortion corrected projections. Spectrally corrected images were then reconstructed from the corrected projections using FBP and denoised using joint BF[13, 14]. We performed basis material decomposition into CS, PE, and I maps.

4.4.2 Result

Our simulation results show that the distortion correction with an ANN performed notably well in correcting the distortion in our test phantom and effectively recovered the K-edge of iodine at \[ \sim 34 \text{ keV} \] (Fig. 4.5). Due to lack of space, we only show the spectral CT images between 28 and 41 keV that includes the iodine K-edge. The ANN distortion correction provided limited denoising. However, some artifacts can be seen at the lower energy bin images. Joint BF was applied to the images before decomposition to further reduce noise.

Using the true mass attenuation coefficient spectra of CS, PE, and I as decomposition basis, it is evident that without distortion correction the spectral decomposition could not provide any meaningful result (Fig. 4.6). Once distortion correction was applied, the improvement in material decomposition was striking. All vials containing iodine were clearly separated from water and the PLA container, and the RMSE of the material decomposition was reduced by 79% compared with the uncorrected result. The contrast-to-noise-ratio (CNR) computed in the iodine map image was
Figure 4.5: Comparison of spectral images before and after applying ANN distortion correction showing recovery of the iodine K-edge at 34 keV with the correction. Also remarkably improved with the distortion correction, enhancing the iodine detectability to 6 mg/ml in the corrected case from 10 mg/ml in the uncorrected case (Fig. 4.7). The average error in the measured iodine concentration was 15% following correction.

4.5 Phantom Data

4.5.1 Method

Similar to the simulation study, our experiment was performed in two steps: (a) training/calibration step using the training phantom and (b) application of the ANN on a test phantom, as shown in the flow chart in Fig. 4.2. The ANN training process...
used a set of raw, distorted projections acquired with our PCXD and a corresponding set of ideal projections without distortion obtained using the 3D digital phantom as a training target. As input to our ANN training, a set of 90 distorted projections over 180 degrees were acquired by scanning our physical phantom with vials containing water and 1, 3, 5, 7, 9, or 11 mg/ml of iodine solution (Fig. 4.3). From the acquired projections, we reconstructed images using FBP at each energy and averaged them to form a less noisy energy averaged image. We then performed an image registration between the digital phantom and the energy averaged image using MATLAB’s phase correlation-based image registration algorithm. The corresponding target set for the training was synthesized from the registered digital phantom using the ideal x-ray spectrum and material attenuation generated by Spektr [37] and the NIST XCOM database [45]. The training set was appended with another set of 90 distorted
Figure 4.7: CNR plots evaluated for each vial with concentration from 2 to 14 mg/ml (the mean value of the 1st vial at the upper left corner, which contains water only, was used as the background value for CNR calculation). The minimum iodine detectable concentrations are found using the intersection with the CNR=5 horizontal line.

projections reprojected from the denoised version of the raw images using joint BF and was matched to the same target to provide a less noisy estimate of the input data. After the ANN was trained, it was applied to a different test phantom fabricated with the same material but with different geometry (Fig. 4.3).

4.5.2 Result

The experimental result further validated the ability of the ANN to perform distortion correction after training with 180 projections (90 raw noisy projections and 90 re-projections of BF filtered images) of a tomographic calibration scan. The test phantom result is shown in Fig. 4.8. The iodine K-edge recovery at 34 keV and
Figure 4.8: The left column shows a picture of the 3D printed test phantom containing 0, 2, 4, 6, 8 and 10 mg/ml of iodine in water (labeled 1-6, respectively) and an axial slice through the phantom showing the corresponding ROIs. The right column shows raw spectral images acquired by our PCXD and reconstructed with FBP before (first row) and after (second row) applying the distortion correction obtained from the trained ANN. After the distortion correction, bilateral filtration was applied to further reduce noise (third row). Without correction, the iodine K-edge was smeared out over multiple energy bins. Once distortion was corrected for, the K-edge was notably recovered at 34 keV. The noise level was also greatly reduced.

noise reduction can be noted in the distortion corrected and denoised results. As shown in both Figs. 4.8, 4.9 and 4.10, the iodine K-edge was smeared out in images reconstructed from spectrally distorted projections, but it was clearly recovered by distortion correction at the correct energy around the K-edge (i.e. ~34 keV). Fig. 4.9 presents the line attenuation plots measured for iodine vials of 3 different concentrations, water and PLA with and without distortion corrections. While the distortion correction brings back the K-edge of iodine, some bias for water and PLA are also noted.

As Fig. 4.11 shows, the performance of material decomposition was severely limited by the spectral distortion, resulting in misclassification of iodine into PE and
Figure 4.9: Measured attenuation in each vial (vials 1,2,4 and 6 in Fig. ??) and an ROI containing PLA phantom material before (dotted lines) and after application of ANN distortion correction.

CS and in underestimation of the iodine concentrations. Consistent with our simulation results, the improvement in material decomposition with our ANN distortion correction is evident. With distortion correction, the mean iodine concentrations measured in each vial (labeled 2 to 6 in Fig. 4.8) are 2.28, 3.49, 5.13, 7.29 and 8.32 mg/ml, respectively, compared to 1.53, 1.67, 1.85, 2.61 and 3.69 mg/ml without correction (Fig. 4.12). The mean relative error in iodine concentration estimation was reduced to 13% with the distortion correction from 56% without correction, a 43% improvement in material decomposition accuracy.
Figure 4.10: Measured enhancement (HU) per mg/ml of iodine solution from the distorted (red), spectral distortion corrected (blue) images and modeled reference values (green). The K-edge enhancement from iodine at 34 keV was notably recovered with the ANN distortion correction matching the expected true value.

4.6 Ex-vivo Mouse Data

4.6.1 Method

To further illustrate the use of the ANN distortion correction, a C57BL/6 mouse was scanned using our custom PCXD based micro-CT system. The mouse was injected via tail vein with 0.3 ml of a liposomal iodinated contrast agent [44]. Next, the animal was euthanized and scanned using full-spectrum CT at the same parameters as in the experimental phantoms. The full-spectrum projection data of the mouse was then fed into the ANN trained using the phantom described above to perform spectral distortion correction. The distortion corrected projections were then reconstructed using FBP and denoised via joint BF. Material decomposition was done on the mouse data in the same manner detailed in Section 4.3. using a material sensitivity matrix.
measured from the training/calibration phantom data for the corresponding with and without distortion correction cases. To provide better anatomical reference for comparison, the same mouse was scanned at higher resolution using another PCXD detector (Pilatus 300k CdTe detector from Dectris Ltd; Baden, Switzerland [46]) with a single threshold set at 20 keV. This detector has a pixel size of 172 m x 172 m. We note that we used this PCXD only to provide an image for anatomical reference and that its spectral capabilities were not relevant for this study. The x-ray source for this high resolution scan was a Thermo Scientific PXS10 MicroFocus x-ray tube [47] used at 80 kVp, 251 µA and with an integration time of 10 ms per exposure.

4.6.2 Result

Finally, Figs. 4.13 and 4.14 show our murine experimental results. A high resolution scan is shown in Fig. 4.13 to provide anatomical reference to the lower resolution full
Figure 4.12: Comparison of measured iodine concentrations (in each vial shown in Fig. 4.8) from the iodine images with (blue) and without (red) distortion correction. The material decomposition was greatly improved with distortion correction resulting in more accurate iodine concentration estimation.

spectrum CT scan. An axial slice across the heart of the mouse was reconstructed in full-spectrum mode and denoised using our joint BF, providing high fidelity images even in the extremely photon-starved lower and higher energy bins. The iodine in the blood pool can be clearly seen as enhancement in the heart. However, the K-edge contrast was smeared out along the energy dimension if the distortion is left uncorrected. A comparison between the spectral distortion corrected and uncorrected images validates the iodine K-edge recovery with distortion correction at \( \sim 34keV \). Fig. 4.14 highlights the material decomposition improvement with our ANN based spectral distortion correction. Two solution vials attached to the mouse, containing water and 5 mg/ml of iodine solution respectively, were accurately identified by the material decomposition of the distortion corrected data. However, this contrast is
Figure 4.13: Summary of spectral distortion results in a mouse scan. 2D cross sectional slices across the heart of the mouse are shown on the left corresponding to energy bins from 28 keV to 41 keV. The images were reconstructed using FBP from distorted projections (first row), distortion corrected projections (second row), and the denoised version of the distortion corrected image (third row) produced using joint bilateral filtration. A high resolution scan is shown at the top-right corner to provide anatomical reference showing an average slice across the heart of the mouse to match the resolution of the lower resolution full-spectrum image. The enhancement in the heart corresponds to the presence of iodine in the blood pool injected through the tail vein of the mouse before the mouse was euthanized. The loss of K-edge contrast in the spectrally distorted images was recovered by the ANN distortion correction, as highlighted in the jump of enhancement between the 33 and 34 keV energy bins (lower right).

not as clear in the case of uncorrected data, where both water/tissue and iodine are clearly misclassified. With ANN distortion correction, the CS and PE physical basis images are relatively homogeneous throughout the mouse body, with attenuation values near the expected values for water. Without distortion correction, the CS component was heavily underestimated, causing overestimations in the PE and iodine basis images.
Figure 4.14: Material decomposition of the mouse data. Without distortion correction (first row), more soft tissue was misidentified as iodine. After distortion correction (second row), the misclassification was improved as shown in relatively homogeneous CS and PE images. The iodine map appears to be more accurately identified at locations corresponding to the heart of the mouse (red arrow). The composite images (shown on the right) show the iodine map (green) superimposed on the water image (black and white) without (first row) and with (second row) distortion correction. The vial containing 5 mg/ml of iodine was accurately identified after distortion correction with a measured concentration of 4.7 mg/ml.
Conclusions

The objectives of this work were to develop and demonstrate novel ANN based techniques to compensate or correct for spectral distortion in PCXD based spectral CT. We have successfully implemented and compared two distortion compensation techniques and one distortion correction technique for PCXD-based spectral CT.

We implemented the projection decomposition using MLEM, as proposed in [6], which enabled the incorporation of a parametric distortion model to compensate for the spectral distortion. The results from this simulation validated the potential of using a distortion compensation technique to improve material decomposition accuracy. However, this method requires a very accurate parametric distortion model to provide sensible results, which can only be obtained through synchrotron measurements as used by Schlomka et al. in [6].

To overcome this need for synchrotron measurements, we proposed and implemented an alternative distortion model derived from an ANN learning algorithm to be used with the same projection decomposition technique. The ANN-based distortion model can be derived from a CT calibration scan using a 3D-printed phantom, and provides a great advantage over the parametric model. Although we believe the
ANN may not provide a perfect model of the distortion, the resulting decomposition using this ANN-based distortion model proved to be more robust than and greatly outperformed the use of a parametric model in the presence of noise or imperfection in fitting the model. Although the PCXD distortion models are trained with full-spectrum CT data, the application of the ANN model does not require that full-spectrum CT is performed every time. Instead, a 4- or 6-energy bin acquisition, using the built-in capabilities of the PCXD, can be used. The detector response function can be binned according to the acquisition.

Lastly, we successfully implemented a novel ANN-based distortion correction algorithm to directly undo the spectral distortion in photon-starved, full-spectrum PCXD data to improve material decomposition performance. Full spectrum CT could be seen as the CT equivalent of 3D histology with multiple heavy metal stains. The proposed technique trained a neural network to learn the non-linear relationship between the distorted spectra recorded by the PCXD and their corresponding ideal, distortion-free spectra without requiring a specific model of the detector distortion. Using 3D modeling and 3D printing technology, the ANN training was performed as a calibration step based after which the trained ANN can be used to correct for distortion in any subsequent scans on the same system and the same scanning parameters (kVp, mAs) and basis materials. This correction scheme puts most of the computational stress on the calibration (training) process, while the distortion correction operation itself requires negligible computation. This allows seamless integration into any existing imaging frameworks without imposing additional constraints. Since our ANN based distortion correction is done on projection data, the resulting distortion corrected projections can be used with any reconstruction and material decomposition algorithms. Given that our technique does not require accurate knowledge of the spectral distortion model, the strenuous synchrotron measurements and calibration required with other techniques such as in [6] can be eliminated. Additionally,
our novel joint bilateral filtration denoising algorithm [13, 14] further augmented our ability to deal with extremely noisy spectral CT data at dense energy sampling as in full spectrum CT.

The results demonstrate the feasibility of using an ANN to correct for spectral distortion in full-spectrum CT imaging, leading to improved spectral material decomposition. The simulation study shows the improved iodine detectability from $\sim 10 \text{mg/ml}$ with distortion to $\sim 6 \text{mg/ml}$ with distortion correction. The experiments validated the technique and applicability of the ANN trained on a 3D printed phantom to undo the distortion in another phantom with distinctly different geometry and in a mouse.

The limitations of our correction technique include some bias added by the distortion correction (see Fig. 4.9), causing the water attenuation spectrum to show a small discontinuity at 34 keV and making it appear to contain a K-edge material (i.e. iodine). This could lead to inaccuracy in material concentration measurements. However, the magnitude of this bias (less than 1 mg/ml equivalent of iodine) is well below the level of iodine concentration we could detect, making its contribution to iodine misclassification a rather small background in the iodine image.

Although we have focused here only on iodine (the most commonly used material in CT contrast agents), in theory, the same technique could be used to image multiple K-edge materials by simply extending the training data set to include more K-edge materials either by addition of the new materials in the same training phantom or by appending additional phantom scans containing the new materials. However, with multiple probes other limitations may arise including the proximity between their K-edges, position of the K-edges relative to source spectrum, and the very large variation of photon flux in different energy bins depending on the source spectrum making it a great challenge to choose a source spectrum that is optimized for multiple K-edge materials. We plan to explore the limits of our ANN-based distortion correction.
corrections with multiple contrast agents in future work.

This work explored and demonstrated the feasibility of full-spectrum CT with 1 keV energy sampling which has rarely been attempted before. Previous approaches binned the data into 4 or 5 coarser energy bins to exploit the benefit of lower noise level but at the cost of lower energy resolution which could limit the accuracy of the material decomposition. Our correction technique aimed to fully exploit the potential of full-spectrum energy information by over sampling the energy resolution. However for such a case, photon starvation becomes a challenge. Our success in applying ANN based distortion correction greatly benefited from joint BF based denoising [13, 14]. Further work can be done to improve on our technique, including optimization of the ANN architecture and the choice and amount of training data to control the bias in correcting for distortion in non K-edge materials.

In conclusion, we found that a model-based projection decomposition technique can provide a way to compensate for PCXD distortion to improve material decomposition, but requires a very accurate parametric distortion model. Our ANN-based distortion modeling technique provides a more practical and convenient way to obtain a reliable distortion model that proved to be more robust than the parametric model. We have also proposed and demonstrated the use of a novel ANN-based distortion correction, which in conjunction with a bilateral filtration denoising, provides an alternative to improve material decomposition in spectral CT. By combining the two tools, we were able to address two of toughest challenges facing PCXD-based spectral CT and to apply the framework to improve quantitative material decomposition accuracy. Given the computational efficiency with which the ANN can be applied to projection data, the proposed scheme can readily integrated into existing CT reconstruction pipelines.
Bibliography


