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Implementation of material decomposition using an EMCCD and CMOS-based micro-CT system

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Abstract

This project assessed the effectiveness of using two different detectors to obtain dual-energy (DE) micro-CT data for the carrying out of material decomposition. A micro-CT coupled to either a complementary metal-oxide semiconductor (CMOS) or an electron multiplying CCD (EMCCD) detector was used to acquire image data of a 3D-printed phantom with channels filled with different materials. At any instance, materials such as iohexol contrast agent, water, and platinum were selected to make up the scanned object. DE micro-CT data was acquired, and slices of the scanned object were differentiated by material makeup. The success of the decomposition was assessed quantitatively through the computation of percentage normalized root-mean-square error (%NRMSE). Our results indicate a successful decomposition of iohexol for both detectors (%NRMSE values of 1.8 for EMCCD, 2.4 for CMOS), as well as platinum (%NRMSE value of 4.7). The CMOS detector performed material decomposition on air and water on average with 7 times more %NRMSE, possibly due to the decreased sensitivity of the CMOS system. Material decomposition showed the potential to differentiate between materials such as the iohexol and platinum, perhaps opening the door for its use in the neurovascular anatomical region. Work supported by Toshiba America Medical Systems, and partially supported by NIH grant 2R01EB002873.

Keywords

Material decomposition; dual-energy CT; spectral CT; neurovascular intervention

1. INTRODUCTION

Spectroscopy methods for material analysis have led to greater understanding of material identification and behavior. The implementation of these advances into medical imaging has been delayed by detector and x-ray source limitations. Until recently, the single-energy CT scanners have been the gold standard for patient image acquisition due to its ability for 3D visualization of internal structures. However, this approach is not optimal due to measurement errors related to the inability to differentiate x-ray photons with different energies. Spectral CT can eliminate these errors, thus allowing differentiation of materials with similar attenuation properties, which is nearly impossible with current technologies¹.

Recent advances in detector technologies and software can allow for the translation of such spectroscopic methods to clinical medical imaging.

In particular, neurovascular interventionists have great need for such a novel imaging technique. Commonly used materials in the neurovascular anatomical region not only lead to imaging errors, but also have poor contrast resolution, which could lead to misdiagnosis of conditions in the region. Materials that can have this problem include embolization agents (EA), platinum coils, iohexol contrast agent, and tumors. The importance of these specific materials and pathologies is that they are often found during neurological interventions such as aneurysm and arteriovenous malformation (AVM) treatment. The EA contains tantalum powder mixed in with it for visualization under fluoroscopy and other imaging techniques² that use x-ray attenuation for contrast. This certainly works when the EA is the focus of the imaging, yet it can lead to errors during future visualization of the same region during image acquisitions. These errors are thought to be solvable using spectral CT.

An excellent example for the motivation of material decomposition can be found in Figure 1. The image shown is of the neurovascular anatomical region, and shows a case where single-energy CT is unable to properly differentiate between materials. A cerebral aneurysm is being treated with a platinum coil (red arrow), and it is difficult to differentiate between the platinum coil and the iohexol contrast agent used for visualization. It is quite clear that a single-energy integrated CT scan does not give someone who is viewing the image much in terms of contrast resolution. The iohexol contrast agent and the platinum are difficult to distinguish between using a single-energy CT scan. Material decomposition can be used to obtain more information regarding the imaged region.

Two scans of the object are taken – one at low beam energy, and one at high beam energy. A material's x-ray attenuation coefficient is a function of the energy of those x-rays. Two materials can be discriminated based on how their level of x-ray attenuation changes as the energy of the ray change. Figure 2 shows how the attenuation of various materials changes with changing x-ray beam energy. Material decomposition is a process that can utilize this DE micro-CT information, and display reconstructed slices of the scanned object by the fraction each voxel is made up of simpler materials, called basis materials. In this way, visualization of specific portions of a region of complex anatomy can be improved.

In the literature, there are many implementations of material decomposition using different types of CT image acquisition techniques^{4, 5} and using images of different portions of the body^{6, 7}. The application of these methods to micro-CT and region of interest high resolution imaging for neurovascular disease recognition was investigated with this work, as well as any potential detector dependencies that the method may possess.

Our group has researched and published about the potential for the use of high-resolution region-of-interest (ROI) fluoroscopic detectors in the context of endovascular interventions^{8, 9, 10}. The use of the highest resolution images possible during an endovascular intervention is important, as it provides the most accurate visualization of the anatomy operated on, ensuring the highest chance of a positive outcome for the patient. Additionally, the use of the ROI component reduces the dose the scanned object receives from the imaging

during the procedure, without reducing the image quality of the considered operating region. Both the principles of high-resolution and ROI can be applied to static imaging of the considered region as well¹², improving the quality of the images while reducing the dose to the patient.

The assumption material decomposition makes regarding materials is that an unknown material can be represented as fractions of other materials, as related to the attenuation coefficient of that material at the acquisition energy used. If the claim is made that the basis materials are the only materials that make up the unknown material X, the decomposition process is carried out via the solving of a system of three equations with three unknowns using each voxel of the reconstructed volume material decomposition is carried out on. The system can be found in Equation 1; where $\mu_{X,LokVp}$ is the considered voxel's value in the acquired slice at the low beam energy, $\mu_{X,HikVp}$ is the considered voxel's value in the acquired slice at the high beam energy, $\mu_{1,2,3|LokVp}$ is the voxel value of a pure amount of the basis material considered at the low beam energy, $\mu_{1,2,3|HikVp}$ is the voxel value of a pure amount of the basis material considered at the high beam energy, and $c_{1,2,3}$ is the fraction each basis material makes up the considered voxel.

$$\begin{aligned} \mu_{1,LokVp} \times c_1 + \mu_{2,LokVp} \times c_2 + \mu_{3,LokVp} \times c_3 &= \mu_{X,LokVp} \\ \mu_{1,HikVp} \times c_1 + \mu_{2,HikVp} \times c_2 + \mu_{3,HikVp} \times c_3 &= \mu_{X,HikVp} \\ c_1 + c_2 + c_3 &= 1 \end{aligned} \quad (1)$$

Each voxel value is input to the system as μx at either low or high kVp. $\mu_{1,2,3|Lo,HikVp}$ is the voxel value at low or high kVp of a calibration amount of one of the basis materials the voxel material is decomposed into, and $c_{1,2,3}$ is the fraction that each basis material makes up the unknown material in the considered voxel. The c terms are the three unknown solved for with the system. The calibration sample contains a pure amount of each of the basis materials, and must be included somewhere in the reconstructed slice of the scanned object. Following each slice's processing with this algorithm, the slice is redisplayed using the c values from each voxel, one for each basis material. Each redisplayed voxel's value is equal to a linear mapping of the value of c. The calibration sample and any other pure region of the basis material will show up as maximum intensity. This intensity will drop when less of the basis material is present in the considered voxel, dropping to zero when there is none of the basis material present. In this way, a slice of image data filled with different unknown materials can be redisplayed as percentages of known materials, potentially giving a clinician viewing the images more information regarding the anatomical region being considered.

2. MATERIALS AND METHODS

There were two indirect detector systems used as part of this investigation, an 8 μ m pixel electron multiplying CCD (EMCCD) detector assembled by our group, and a Teledyne DALSA 49.5 μ m pixel complementary metal-oxide semiconductor (CMOS) detector

(Teledyne DALSA, Waterloo, On, Canada). Both detectors utilized a CsI scintillation phosphor of different thickness, and were coupled to a micro-CT unit constructed by our group for the acquisition of pre-clinical image data. Both of these detectors utilize the principles of high-resolution imaging, as well as ROI capabilities for dose reduction to the scanned object.

The first detector investigated was the EMCCD detector. In the process of carrying out a decomposition, it may be optimal to acquire the low-energy scan data using a beam energy below 30 kVp. This could occur in cases where the k-edge of a material happens to be below 30 keV. A CCD-based CT detector can be ineffective at visualizing the scanned object at such conditions due to the readout noise introduced to the system by the output conversion process being at the same magnitude as the image signal. This leads the operator to select higher beam energy for the low energy scan, which can be non-optimal for decomposition of a wide range of materials from an image.

An EMCCD-based CT detector utilizes pre-readout signal amplification (Figure 3), and can be operated effectively at a wide range of x-ray intensities, including the low energies. The multiplication register, something that a standard CCD lacks, carries out this pre-readout signal amplification. The multiplication register works similar to an avalanche photodiode¹³, in that the signal in the form of a charge packet is passed element to element in the multiplication register. At each transfer, there is a small amount of gain applied on the signal, approximately 3%. There are many elements in the register, so many transfers of the charge packets. At the end of the signal amplification step, the total gain on the signal can be several orders of magnitude. The EMCCD detector utilized a 100 μm thick CsI phosphor.

The second detector that was investigated is the CMOS detector. The operation of the CMOS detector is similar to the EMCCD, in that the image signal is converted to a charge, and read out as a voltage. An important difference may be important in the context of material decomposition; the CMOS system used does not possess the same levels of pre-readout amplification that can be applied on the image data, hence the output signal amplitudes will be lower. This reduces the sensitivity of the detector system when a low kVp beam is selected, and may inhibit the use of beam energies below 30 kVp to acquire image data using the CMOS, as the tube output is too low at that beam energy for the sensor. The potential for this will be investigated. The CMOS detector utilized a 300 μm thick CsI phosphor.

Projection data of the scanned object was first acquired at the low beam energy, followed by the high beam energy. Following the acquisition of the two sets of projection data, axial slices of the scanned object were computed. This process was performed using a modified¹⁴ FDK cone-beam CT reconstruction algorithm¹⁵. To preserve the one-to-one position mapping required by the decomposition process, the same reconstruction parameters are selected for both reconstructions. Those parameters include the voxel size, convolution kernel size, and reconstructed volume length. Following the reconstruction, slices were passed on for decomposition.

Every slice that is being reconstructed is processed using the decomposition algorithm. The process that is followed to perform the decomposition can be found in Figure 4, and is based off of a paper by Friedman *et al*¹⁶.

The first step of the decomposition is to constrain the process to a specific structure in the reconstructed slice. If the specific structure being decomposed is a small region of the input reconstructed slice, it is possible to specify that region to quicken the decomposition process by reducing the number of voxels that are processed.

The second step of the decomposition process is to specify the locations of the calibration materials in the reconstructed slices. Recall from Equation 1 the terms $\mu_{1,2,3|hi,lo}$, the mean intensity value of the voxels in a pure amount of each of the basis materials. This amount is specified by taking an average of voxel values in an ROI specified on the calibration sample. This value is set as the terms $\mu_{1,2,3|hi,lo}$.

The third step of the decomposition process is to solve the system of equations contained in Equation 1 for the values of c for all of the basis materials. Recall that c is the fraction of each reconstructed voxel containing the basis material. At each voxel, the system is solved for each c value. These c values are what are used to re-display the slice in the space of each of the basis materials.

The fourth step of the decomposition process is to actually re-display the slice. The value of the re-displayed voxel is computed from the c value, multiplied by maximum image value. A pure amount of a material will show up as maximum image intensity. Some combination of material will show up as an image intensity equal to the computation of the c term multiplied by maximum image intensity, and none of the material will show up as an image intensity of zero. In this way, two input slices of reconstructed data, one obtained using a high kVp and one obtained using a low kVp, are re-displayed in terms of the makeup of the material by the three basis materials.

As output from the decomposition process, decomposed slices of image data are obtained. In order to quantify the performance of the decomposition process and to make it easier to tune the algorithm for better decompositions, there needs to be a method for the quantitative assessment of the decompositions. The method that was selected is the Normalized Root Mean Square Error (NRMSE) metric¹⁷. The NRMSE metric measures differences between expected and observed values of a system, normalized by the intensity of the measurements. This metric is defined in Equation 2.

$$\%NRMSE = \frac{100}{f_{\max}^{\text{meas}} - f_{\min}^{\text{meas}}} \sqrt{\sum_{j=1}^v \frac{(f_j^{\text{ref}} - f_j^{\text{meas}})^2}{v}} \quad (2)$$

%NRMSE is the percent normalized root mean square error metric. The summation of the interior terms is performed on every voxel in the redisplayed slice. $f_{\max}^{\text{meas}}$ is the maximum

value in the slice. $f_{\min}^{\text{meas}}$ is the minimum value in the slice. f_j^{ref} is the expected value of the considered voxel. f_j^{meas} is the measured value of the considered voxel. v is the total number of voxels in the slice. For this type of quantitative assessment, there is prior knowledge of the object that is imaged and decomposed. This allows us to get f_j^{ref} and input it into Equation 2, allowing the comparison between what the decomposition is telling regarding the material makeup of the scanned object with the object's "true" material makeup. An accurate decomposition is one that shows agreement with prior knowledge of the scanned object, thus will have a small value for %NRMSE.

The DE micro-CT data was acquired using different low/high beam energies, due to different characteristics of the detector system used. When the EMCCD detector was used, data was acquired using 25 kVp and 70 kVp. When the CMOS detector was used, the low energy had to be increased to 35 kVp due to the lower sensitivity of the detector. The high energy was kept the same. Both detectors were coupled to a micro-CT system constructed by our group.

3. RESULTS

The first decomposition that was carried out can be found in Figure 5. The scanned object was a phantom with channels filled with either iohexol contrast agent or water. This decomposition was between iohexol contrast agent, water, and the 3D-printing material that comprised the phantom. Projection images were acquired using the energy integration mode of the micro-CT. Calibration samples were taken using one of the channels filled with basis material, leaving the remaining channels to be used for the %NRMSE assessment.

The second decomposition that was carried out can be found in Figure 6. The difference between this and the first decomposition is that the phantom used had slightly smaller diameter channels, and the phantom channels were either filled with iohexol or left empty. The decomposition in this case was between the iohexol, the air, and the 3Dprinting material.

It was through these two decompositions that the NRMSE was computed. The results of the computation of this metric can be found in Table 1.

The CMOS detector was also utilized for the acquisition of DE micro-CT data used for material decomposition. The same two decompositions carried out using the EMCCD were also carried out using the CMOS detector. The first of which, between iohexol, water, and the 3D-printing material, can be found in Figure 7.

A second decomposition was carried out using the CMOS for image acquisition, where the phantom channels were filled with iohexol, or left empty. The decomposition shown in Figure 8 was between the iohexol, the air, and the 3D-printing material.

Once again, NRMSE was computed for the different materials using the decomposition found in Figures 7 and 8. The values of this computation can be found in Table 2.

Additionally, a trial was carried out using materials specific to a neurovascular intervention using the CMOS detector. The channels of the phantom were filled with iohexol contrast agent, a platinum coil, and water. The results of this decomposition can be found in Figure 9. %NRMSE computation using this decomposition can be found in Table 3.

4. DISCUSSION

The decomposition process is effective at picking out iohexol from the phantom regardless of the detector used to acquire the DE micro-CT image data, since the iodine in the contrast agent has different attenuation characteristics from air, water, and the 3D-printing material. There is a large gap between the materials on the attenuation curves with respect to varying tube voltage, enabling an effective decomposition. In a case such as this, material decomposition processing is not necessary. There is enough contrast at a single energy CT scan to be able to tell the difference between the iohexol and the other materials in the phantom. It becomes more challenging when considering the other materials, namely the decomposition of water and from the 3D printing material. When the EMCCD detector was used, the two materials were difficult to differentiate between in the slice seen in Figure 5a. The decomposition process is able to pick out the water channels, with the error typically around the regions of the beam hardening artifacts. Artifact reduction is essential to the success of the decomposition. Regions of the phantom that have streaks going through them throw off the process. This is seen in Figures 5d and 6d. The 3D-printing material is properly decomposed except in the regions of the streaks. Interestingly, the streaks show up similarly to air in Figure 6c, indicating that the process is confusing the air and the beam hardening artifact. This problem can be solved with more aggressive filtering of the x-ray beam¹⁸, or the use of a thicker phosphor. The EMCCD detector utilized a 100 μm phosphor to ensure the highest resolution possible, yet this thin phosphor led to more of the streaking artifacts.

Qualitatively, it appears that the iohexol is most successfully decomposed from the phantom. In the iohexol-space slice, there is little signal from regions other than where the iohexol-filled channels are, and it is maximum intensity at the regions that are pure iohexol. The water and air slices are more impacted by the beam hardening artifacts, and look less successfully decomposed, as indicated by the NRMSE metric shown in table 1. The iohexol map has the lowest % NRMSE at 1.8%, water is the next highest at 5.2%, air is the highest with the most error at 7.8%, and the printing material is 6.5% error. Even with the air being the highest % NRMSE, it still is on the same order of magnitude as other reported values of %NRMSE in the literature¹⁷ when the metric was used in the context of material decomposition.

When the CMOS detector was used to acquire the DE micro-CT energy image data, the iohexol again was successfully differentiated from the scanned object (Figures 7 and 8). Lower Z materials, such as the water and air were more challenging. In all measurements, the CMOS detector had higher %NRMSE values than the EMCCD detector, especially when the lower Z materials were considered. The iohexol %NRMSE was only 29% higher than the EMCCD measurement, and only 31% higher for the 3D-printing material, yet for air it was 136% higher, and 150% higher for the water. The air, water, and 3D-printing material

have little in contrast resolution at the energies used for the image acquisition, and are not successfully differentiated between following the material decomposition process. The streaking artifacts were not as prevalent in the CMOS acquisitions as the EMCCD acquisitions, potentially due to the thicker phosphor being used in the CMOS detector system.

In the case of Figure 9, the materials included are more similar to those used during a neurovascular intervention. Both platinum and iohexol were included in the phantom along with water. Both the iohexol and platinum are high Z materials, and following the trend started during the previous decompositions, are decomposed from the rest of the phantom with low %NRMSE (Table 3). The lower Z water was similarly challenging to differentiate as with the trials shown in Figures 7 and 8.

A limitation on the method described in this work is the use of basis material characteristics derived from the actual acquisition. Hence, the mixing of basis materials within a voxel is not considered and would require a more complex analysis.

There are multiple methods that researchers have developed to obtain the DE spectral CT data. Siemens developed a system that employs two tubes operating at a different voltage, and two detector panels¹⁹. General Electric has a system that uses one tube with rapid kVp switching, and one detector panel²⁰. Philips has a system that uses one tube with a single tube voltage, and a stack of two detector panels²¹. The front panel attenuates the low energy photons; the back panel attenuates the high energy photons. The method used to obtain the data in this work was less complicated in that separate complete acquisitions are carried out for each beam energy. Due to the use of higher resolution detectors; however, this approach may be more applicable to higher resolution cone-beam CT applications.

An important consideration for future application is the apparent increase in dose to the scanned object or patient as a result of the DE micro-CT acquisitions. Future solutions to this problem may involve the use of single photoncounting detectors capable of acquiring spectral CT image data. Such detectors with high resolution used in cone-beam CT are under development and hold promise for the future. Nevertheless, the risk vs. benefit assessment for this DE mode will have to be considered for future clinical applications.

5. CONCLUSION

This project was involved with the investigation of the use of material decomposition on images taken of a phantom with neurovascular-like anatomical regions. Often, the endovascular devices used during neurovascular intervention can render the region difficult to image using a single-energy CT scan. The use of DE micro-CT data utilizes the varying attenuation coefficient of materials as beam energy changes, and can obtain information that leads to better differentiation of structures in the neurovascular anatomical region.

Preliminary results show promise. The two goals of this study were to study the material and detector dependency of the material decomposition method. In the context of neurovascular intervention, the common materials used include iohexol contrast agent, tantalum, platinum, and the actual vasculature. This work has shown the ability of a material decomposition

process to be able to discriminate between materials such as water and 3D printing material, as well as platinum and iohexol.

Additionally, the use of different detector systems was investigated, including EMCCD and CMOS systems. The accuracy of the material differentiation gauged by the computation of %NRMSE indicates that the different detector systems can be used for material decomposition; however the CMOS detector was limited in differentiation of the low Z materials, possibly due to the decreased sensitivity of that detector at low kVps. Nevertheless, the positive preliminary results appear to warrant further investigation and potential application to clinical development.

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Figure 1. Image of neurovascular intervention showing the difficulty of material differentiation in the region when single-energy CT is utilized. Location of intervention is shown (red arrow).³

Figure 2. Image showing attenuation coefficient of tantalum, iodine, and platinum as beam energy varies¹¹.

Figure 3.

Schematic of EMCCD detector. Note the multiplication register placed before the output amplifier. This carried out the pre-readout amplification of the image data.

Figure 4.

Image showing algorithm that the material decomposition process is carried out using.

Figure 5.

Decomposition from EMCCD-acquired DE micro-CT image data. (a) is a reconstructed slice of the phantom, channels filled with iodine or water. (b) is the slice displayed in the iodine space. (c) is the object displayed in the water space. (d) is the object displayed in the 3D-printing material space. ROIs in (a) taken for calibration samples, black is iodine, yellow is water, blue is printing material. ROIs in (c) are taken for the %NRMSE computation. Note the success of the iodine and water decomposition (b and c), and the streaking artifacts affecting the decomposition in (d).

Figure 6.

Decomposition from EMCCD-acquired DE micro-CT image data. (a) is a reconstructed slice of the phantom, channels filled with iohexol or empty. (b) is the slice displayed in the iohexol space. (c) is the slice displayed in the air space. (d) is the slice displayed in the 3D-printing material space. ROIs in (a) are taken for calibration samples, black is iohexol, yellow is air, blue is printing material. Note the success of the iohexol decomposition (b) and the streaking artifacts affecting the decompositions in (c and d).

Figure 7.

Decomposition from CMOS-acquired DE micro-CT image data, (a) is a reconstructed slice of the phantom, channels filled with iodine or water, (b) is the slice in the iodine map, (c) is the slice in the 3D-printing map, and (d) is the slice in the water map. ROIs extracted in (a) are taken for the calibration samples, black for water, blue for iodine, and yellow for printing material. Note the little differentiation of water in (d).

Figure 8.

Decomposition from CMOS-acquired DE micro-CT image data. (a) is the original slice of the phantom, (b) is the slice in the iohexol map, (c) is the slice in the 3D-printing material map, and (d) is the slice in the air map. ROIs extracted in (a) are taken for the calibration samples, black for iohexol, blue for printing material, and red for air. Note the little differentiation of air in (d).

Figure 9.

Decomposition from CMOS-acquired DE micro-CT image data. (a) is a reconstructed slice of the phantom, channels filled with iodine or platinum or water, (b) is the slice in the platinum map, (c) is the slice in the iodine map, (d) is the slice in the water space. ROIs extracted in (a) are for the calibration samples, black for iodine, yellow for platinum, blue for water. Note the success of the decomposition between iodine and platinum.

Table 1

Results of %NRMSE computation for the EMCCD decompositions. Note the success of the high Z material decomposition relative to the lower Z materials more impacted by the streaking artifacts.

NRMSE (%)	
iohexol	1.8
water	5.2
air	7.8
print mat	6.5

Table 2

Results of the %NRMSE computation for the CMOS decomposition of iohexol, air, water, and printing material. Note the success of the iohexol decomposition, and the challenging decomposition of the air and water.

NRMSE (%)	
iohexol	2.4
air	27.7
water	54.6
print mat	8.9

Table 3

Results of the %NRMSE computation for CMOS decomposition of iohexol, platinum, water. Note success of high Z materials, and the reduced performance of water.

NRMSE (%)	
iohexol	3.1
platinum	4.7
water	37.2