Contrast agent recognition in small animal CT using the Medipix2 detector

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Abstract

Energy resolving capabilities of X-ray detectors like the Medipix2 and the upcoming Medipix3 offer access to spectral information which is a new domain of information in medical imaging.

In conventional CT of a composite object only the cumulative contribution of all involved materials to the attenuation is measurable, but not how much each material component contributes to this attenuation. Therefore, contrast agent can not be distinguished from bone or calcifications. The method of material reconstruction exploits the energy information to determine the partial densities of the involved materials using a Maximum Likelihood approach, i.e. it allows the separation of contrast agent from tissue, bones and calcifications.

We have employed the MARS scanner equipped with a Medipix2 MXR and performed a CT scan of a mouse with iodine contrast agent in stomach and bowel. The method allows to separate the iodine contrast agent from all the other absorbing structures. In the iodine image, only the iodine concentration is visible, while the non-iodine (water) image shows all the other tissue structures and bones. The method of material reconstruction was applied to real CT data of a biological sample for the first time.

Key words: X-Ray imaging, computed tomography, bio-imaging, Medipix, photon counting, pixel detector, material decomposition, material reconstruction, K-edge

1. Introduction

The conventional X-ray imaging of a composed object only allows access to the cumulative attenuation, but the contribution of different materials can not be resolved.

Detectors like the Medipix2 [1] with energy sensitive X-ray detection allow new possibilities in quantitative X-ray imaging as the material resolved imaging [2]. This method was applied to computed tomography.

In some situations in medical imaging, it is necessary to obtain two or more sets of images, such as in triple phase liver imaging, or CT angiography where subtraction techniques display the vessls more clearly. We present a method allowing all the required information to be displayed from a single acquisition.

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2. Basic Idea

As spectral information is becoming accessible for X-ray imaging, this additional information can be exploited. The X-ray attenuation coefficient of each component of a compound material varies with the photon energy. ® The basic idea of material reconstruction is to decompose the compound material into its components by the differences in their attenuation spectrum.

2.1. *X-ray Attenuation*

The attenuation of X-rays is energy dependent and differs between different materials. Attenuation can be described by Lambert-Beer's Law:

$$I(E) = I_0(E) e^{-\mu'(E)\, a} \tag{1}$$

$$\text{or} \quad -\log\left(\frac{I(E)}{I_0(E)}\right) = \mu'(E)\, a =: A(E) \tag{2}$$

where $\mu' := \mu/\rho$ is the mass attenuation coefficient, $a := \int \rho(s)\, \mathrm{d}s$ is the projected or areal density along the X-ray

beam and $A(E)$ the absorbance.

2.2. *Basis Materials*

For compound objects the absorbance A may be written as the weighted sum of its material components:

$$A(E) = \sum_k \mu'_k(E) \cdot a_k \tag{3}$$

where k is the index for the basis materials. In a notation discrete in the energy it can be written

$$A_j = \sum_k \mu'_{jk} \cdot a_k \tag{4}$$

with j indexing the photon energy.

The set of linear equations (4) can only be solved for the areal densities a_k of the chosen basis materials, provided the basis, i.e. the mass attenuation coefficients μ'_j of the involved materials are linearly independent. This is in principle true for any two different elements, but is fulfilled better, if the difference in the atomic Number Z is large. For more than two elements, each of the additional elements needs an absorption edge (e. g. K- or L-edge) within the usable energy range of the application [3]. The choice of usable basis materials is not limited to elements. Any compound can be used as long as the set is linearly independent with respect to their mass attenuation spectra.

The projected or areal density of each basis material can then be obtained quantitatively from a maximum likelihood estimation.

3. Material Reconstruction Method

3.1. *Detector Response*

When using a pixelated photon counting detector like the Medipix2, the energy response of the detector due to charge sharing between pixels needs to be taken into account. For known energy response functions to mono energetic irradiation R_{ij}, with index i for the energy deposition and index j for the primary photon energy, the measured energy deposition spectrum m_i is given by

$$m_i = \sum_j R_{ij} s_j$$

where s_j is the spectrum of impinging photons. We have shown in previous work that the response functions can be simulated very accurately, and have been checked by comparision with measurements [4].

3.2. *Maximum Likelihood Method*

The likelihood function indicates how likely a particulary set of parameters (in this case the material composition) of an object is compatible with the observed detector signals. Thus the maximum of this function indicates the one set of parameters that has the highest probability to lead to the given measurement.

Provided the number of photons N_j (following Poission statistics) in an energy channel is high enough to be considered as normally distributed, the likelihood function for the number of photons in an energy channel is

$$\begin{aligned} &L(a_1, a_2, \ldots, a_k) = \\ &= \prod_j \frac{1}{\sqrt{2\pi N_j}} \, \mathrm{e}^{-\frac{\left(N_j - N_{0,j} \exp(-\sum_k \mu'_{jk} a_k)\right)^2}{2N_j}} \end{aligned} \tag{5}$$

Since over the range of the likelihood function the logarithm is a continuous strictly increasing function, values maximising L will also maximise its logarithm $f := \ln(L)$ and minimise the negative $F := -f$. As most of the common algorithms are designed to search for minimum rather than maximum values, we have elected to find the minimum of F. The function to minimise is:

$$\begin{aligned} &F(a_1, \ldots, a_k) = -\ln\left(L(a_1, \ldots, a_k)\right) = \\ &= \text{const.} + \sum_j \frac{\left(N_j - N_{0,j} \mathrm{e}^{-\sum_k \mu'_{jk} a_k}\right)^2}{2N_j} \end{aligned} \tag{6}$$

This function is proportional to the sum of the squared differences between the estimate and the measurement, to minimize it is therefore equivalent to the least squares method.

Including the energy respones of the detector, the negative log-likelihood function becomes

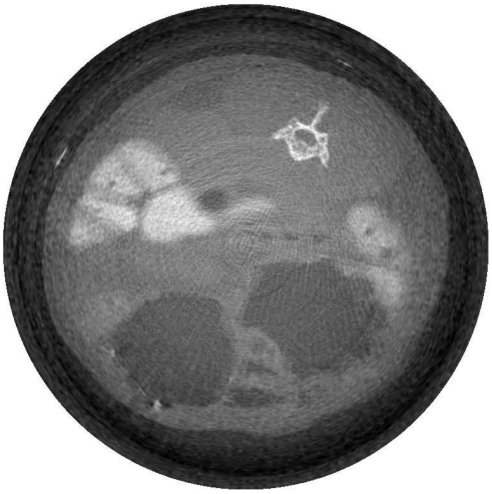
$$\begin{aligned} &F(a_1, \ldots, a_k) = \\ &= \text{const.} + \sum_l \frac{\left(N'_l - \sum_{i=E_l}^{E_{l+1}} \sum_j R_{ij} N_{0,j} \mathrm{e}^{-\sum_k \mu'_{jk} a_k}\right)^2}{2N'_l} \end{aligned} \tag{7}$$

4. Measurements

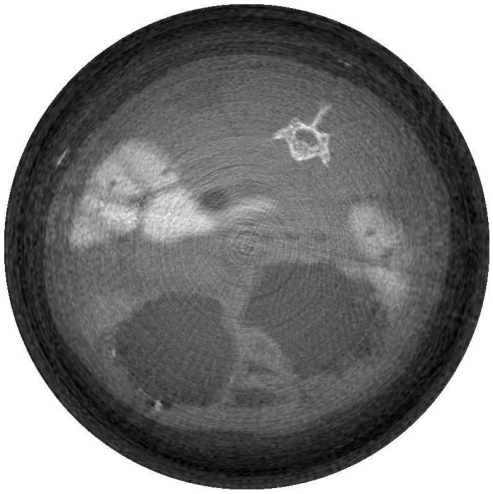
4.1. *Setup*

For the measurements the MARS scanner (Medipix All Resolution System) [5] was used. In this scanner, the Medipix2 (MXR) detector is employed. It has 256×256 pixels and an adjustable energy threshold, i. e. the detector only counts events with an energy deposition above this threshold in the respective pixel. The sensor layer consists of 300 μm silicon.

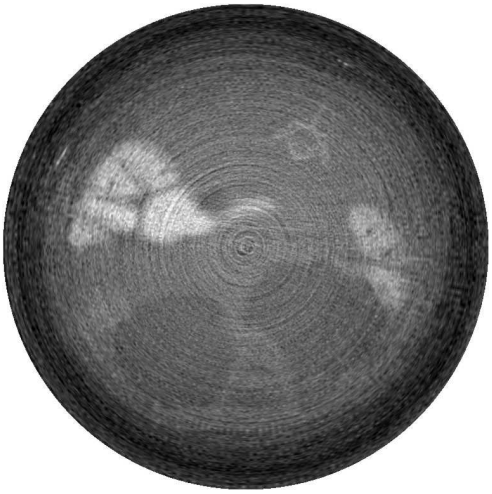
The detector and the X-ray source rotate around the object to acquire the projection images. The projection images were taken at three adjacent positions and put together afterwards, so each projection is 256×768 pixel. 360 projections were taken with an increment of one degree. Furthermore, four different energy thresholds were applied at the Medipix2 detector, in fact at 12, 17, 33 and 42 keV.



(a) threshold at 12 keV

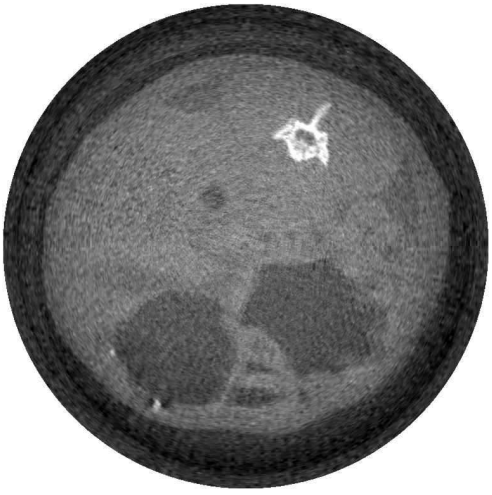


(b) threshold at 17 keV

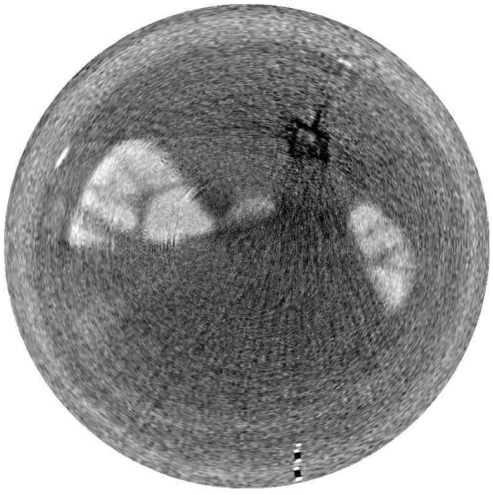


(c) threshold at 33 keV

(d) threshold at 42 keV



(e) Material reconstruction: water image



(f) Material reconstruction: iodine image

Fig. 1. CT reconstructed images for: (a)–(d) the four different energy thresholds at 12, 17, 33 and 42 keV; (e)–(f) the material reconstructed images with basis materials water and iodine.

4.2. *Subject*

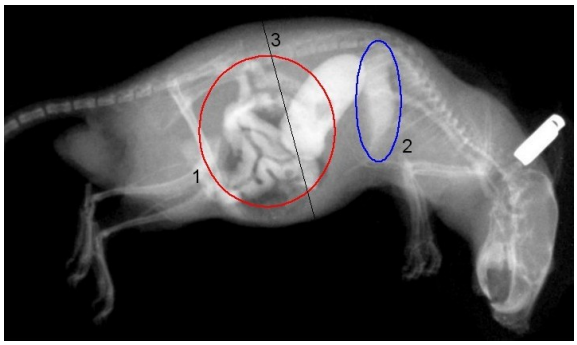


Fig. 2. Plain radiograph of the prepared mouse

A 26.9 g male C57BL/6 mouse was anaesthetised and prepared with the gavage of 0.8 ml iodine containing contrast agent solution (50% iohexol [1] , 50% sterile water) and the post mortem injection of 0.4 ml gadopentetate dimeglumine [2] (gadolinium contrast agent) into the chest. Anaesthesia was induced by Ketamine (37.5 mg/kg) and Domitor (Medetomidine, 0.5 mg/kg) subcutaneously and Euthanasia by intraperitoneal administration of sodium pentobarbital (0.5 ml/kg).

The plain radiograph of the mouse after the contrast agent preparation is displayed in fig. 2 which shows iodinated contrast within the bowel (red circle, number 1), the stomach (the bright oval object between 1 and 2, partly inside 1) and the gadolinium in the pleural space (blue circle, number 2). The black line (number 3) in fig. 2 shows the approximate possition of the CT-plane. It is not the real position, because for the actual CT was taken with the mouse inside a PMMA tube for mounting. The gadolinium is not in the field of view of the CT images.

4.3. *Results*

The reconstructed CT slices for the four different energy thresholds can be seen in fig. 1(a)–(d). They were reconstructed using a standard filtered back projection algorithm. The iodine contrast agent in the bowel can be seen at all four energies, but is hardly distinguishable from structures as bone in the vertebral body in three of them. However, at 33 keV threshold (fig. 1(c)) iodine contrast is distinguishable from bone due to the K-edge of iodine at that energy.

For the material reconstruction a 2×2 rebinning to 128×384 pixels per projection was done to reduce computation time. The basis materials for the material reconstruction were water and iodine, the respective CT slices can be seen in fig. 1(e)–(f) In the water image, both water (soft tissue) and bone is visible and the soft tissue contrast is comparable with the 12 keV and 17 keV images, while the iodine is completely removed from this image. In contrast, the iodine image does not show soft tissue at all, just the expected iodine. In addition, the bone is visible with negative intensity, which is an artefact from the technical point of view, but in this case it is actually helpful, as distinguishing between bone and iodine is one of the purposes of the method.

5. Conclusion

The method of material reconstruction was successfully applied to computed tomography using a small animal scanner equipped with an energy sensitive detector, the Medipix2. It allows iodine contrast agent to be distinguished from all other structures by providing separate images for the (selectable) basis material.

6. Acknoledgements

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References

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