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Department of Biomedical Engineering

Examensarbete

Quantitative Tissue Classification via Dual Energy Computed Tomography for Brachytherapy Treatment Planning: Accuracy of the Three Material Decomposition Method

Examensarbete utfört i Medicinsk Teknik
vid Tekniska högskolan vid Linköping universitet
av

Merve Gürlüler

Linköping 2012

LiTH-IMT/MASTER-EX-- 12/020-- SE



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Abstract

Dual Energy Computed Tomography (DECT) is an emerging technique that offers new possibilities to determine composition of tissues in clinical applications. Accurate knowledge of tissue composition is important for instance for brachytherapy (BT) treatment planning. However, the accuracy of CT numbers measured with contemporary clinical CT scanners is relatively low since CT numbers are affected by image artifacts. The aim of this work was to estimate the accuracy of CT numbers measured with the Siemens SOMATOM Definition Flash DECT scanner and the accuracy of the resulting volume or mass fractions calculated via the three material decomposition method.

CT numbers of water, gelatin and a 3rd component (salt, hydroxyapatite or protein powder) mixtures were measured using Siemens SOMATOM Definition Flash DECT scanner. The accuracy of CT numbers was determined by (i) a comparison with theoretical (true) values and (ii) using different measurement conditions (configurations) and assessing the resulting variations in CT numbers. The accuracy of mass fractions determined via the three material decomposition method was estimated by a comparison with mass fractions measured with calibrated scales. The latter method was assumed to provide highly accurate results.

It was found that (i) axial scanning biased CT numbers for some detector rows. (ii) large volume of air surrounding the measured region shifted CT numbers compared to a configuration where the region was surrounded by water. (iii) highly attenuating object shifted CT numbers of surrounding voxels. (iv) some image kernels caused overshooting and undershooting of CT numbers close to edges. The three material decomposition method produced mass fractions differing from true values by 8% and 15% for the salt and hydroxyapatite mixtures respectively. In this case, the analyzed CT numbers were averaged over a volumetric region. For individual voxels, the volume fractions were affected by statistical noise. The method failed when statistical noise was high or CT numbers of the decomposition triplet were similar.

Contemporary clinical DECT scanners produced image artifacts that strongly affected the accuracy of the three material decomposition method; the Siemens' image reconstruction algorithm is not well suited for quantitative CT. The three material decomposition method worked relatively well for averages of CT numbers taken from volumetric regions as these averages lowered statistical noise in the analyzed data.

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1 Introduction

Cancer is one of the leading causes of death both in Sweden and around the world. In Sweden, the most common form of cancers are prostate and breast cancers [2].

Radiotherapy is often prescribed for treatments of cancer and malignant diseases. The most common form of radiotherapy is external beam radiotherapy. Brachytherapy (BT) is another form of radiotherapy where radiation sources are placed inside or near the area requiring treatment. It is commonly used as a treatment for prostate, breast and skin cancers [19]. The BT technique is used in approximately 5-10% of all cancer cases worldwide [4]. According to a national survey of all radiotherapy practices, 883 and 1283 patients underwent BT in Sweden in 1992 [5] and in 2001 [3], respectively. Treatment of all types of cancer and tumors requires a radiation treatment planning system for the calculation of doses delivered to the patient. Currently radiation treatment planning systems in BT neglect patient anatomy and the variability of tissue compositions. They are based on precalculated dose distributions in unbounded homogenous water medium according to TG-43 recommendations [23]. Recently, more sophisticated algorithms have been developed for dose calculations in BT based on CT-images of the patient. But, lack of detailed information about patient specific tissue compositions still remains a problem. The recently introduced Dual Energy Computed Tomography (DECT) technique in clinical applications has opened new possibilities to determine tissue compositions. This may lead to increased accuracy of BT treatment planning.

At the Linköping University Hospital, a DECT system is available at the Center for Medical Image Science and Visualization (CMIV). The CMIV research center was initiated by Linköping University, the County of Östergötland and Sectra AB in 2002. In 2012, an upgraded version of the Siemens SOMATOM Definition Flash DECT scanner was installed. In this thesis, the updated scanner was used for classifying samples according to a three material decomposition scheme.

1.1 Purpose and Goal

CT numbers are affected by image artifacts such as beam hardening, which bias measured data. One way to estimate the bias is the usage of suitable phantoms. These phantoms can be designed to contain well defined samples, like mixtures of several commonly available chemicals. The main purpose of this thesis is to test the three material decomposition method on the well defined mixtures so that uncertainties associated with this method can be accurately estimated.

1.2 Related Research

To perform tissue classification via computed tomography (CT) and dual energy CT, different methods have been developed. In 1976, Alvarez and Macovski suggested a method to separate the linear attenuation coefficient into contributions from photoelectric and Compton scattering for selected voxels. The idea was based on the fact that the photoelectric effect depends on atomic number, which indicates the composition of the material, and the Compton scattering, which depends on electron density [6].

Schneider et al. (2000) developed a method to determine mass densities and elemental weights of tissues by dividing the scale of CT numbers into intervals. Mass densities and elemental weights were interpolated within each interval [7]. Because of the relationship between these tissue parameters and the CT number, this method was valid for decomposition into two components only. It was relatively good for the extraction of mass densities of skeletal tissues and cortical bone. On the other hand, large errors were observed for soft tissues when describe as composed of only two components.

Yu et al. [8] investigated a pre-reconstruction three material decomposition method using DECT to quantify the concentration of each component in a mixture with known chemical compositions. They used a pre-reconstruction method as it avoids beam hardening artifacts. They found that stability of this method strongly depends on physical properties of the components and x-ray spectra.

Liu et al. (2009) [9] investigated two and three material decomposition methods using DECT. They performed phantom studies using two different phantoms that contained mixtures of water, hydroxyapatite and iron nitrate solutions with varying concentrations of iron and calcium. The authors needed one more criterion to extract three unknown parameters from only two measurements with different spectra. They used the three material decomposition method and the law of mass conservation.

In 2008, A. Malusek, M. Magnusson, M. Sandborg and G. Alm Carlsson developed an iterative reconstruction algorithm for quantitative tissue classification. This project has been improved as follows: In 2010, simulation studies were done with this algorithm that decomposes a soft tissue into three base components: water, protein and adipose tissue. The results of the this study demonstrated that the effect of the beam hardening artifacts can be removed effectively and the mass fractions of each base materials were estimated accurately with this iterative algorithm [32, 33, 34]. In 2010, another study was performed for quantitative tissue classification that includes Monte Carlo simulations to evaluate the effects on absorbed dose distributions. This study indicated that choices of base components play

important role to determine tissue compositions accurately [10]. In 2012, simulation studies were performed for classifying bone (cortical bone and marrow) and soft tissue (water, protein and adipose tissue) and simulated data containing noise were evaluated [11]. This thesis is an extension of the quantitative tissue decomposition method to test and to evaluate the accuracy of the three material decomposition method by using suitable phantoms.

2 Background

2.1 Computed Tomography

A conventional Computed Tomography (CT) scanner provides that the two dimensional internal structure of slices through a three dimensional object is reconstructed from a series of one dimensional x-ray projections of the object obtained at different angles. For each pixel in the reconstructed image, a CT number is calculated which is related to the linear attenuation coefficient for that pixel $\mu(x, y)$ and linear attenuation coefficient for water μ_w according to the following equation:

$$H = \frac{\mu(x,y) - \mu_w}{\mu_w} 1000 \quad (1)$$

CT numbers can be used to characterize tissues. Some typical values of the CT numbers for air and different tissues are given in Table-1.

Table 1 : CT values for different materials [12]

Material	Range (Hounsfield units)
Air	-1000
Lung	-200 to -500
Fat	-50 to -200
Water	0
Muscle	+25 to +40
Bone	+200 to +1000

2.2 Dual Energy Computed Tomography

Dual Energy Computed Tomography (DECT) is a technique that uses two different x-ray spectra (tube voltages) to scan an object. There are different ways to accomplish this in practice. One of the approaches has been developed by Philips [13], its detector system allows extraction of low and high energy spectra during one scanning [14].

Another approach has been developed by General Electrics (GE) that uses fast switching between two tube voltages during scanning [15].

At the Linköping University Hospital, Siemens SOMATOM Definition Flash Dual Energy CT scanner uses still another approach with two different x-ray tubes operating at two different tube voltages, see Figure 1. The tubes are simultaneously rotated around the object. In the figure, the 140 kV spectrum is obtained using an extra tin filter (selective photon shield). This tin filter provides an increased separation between the low and high energy spectra. It also helps to reduce the patient dose compared to using 140 kV without tin filter [16]. Table-2 shows the technical specifications of the Siemens SOMATOM Definition Flash DECT Scanner.

The detector row for the x-ray tube operated at 80 kV is smaller than detector row for the x-ray tube operated at 140 kV. The acquired images at 80 kV register a smaller region of the object than the images captured at 140 kV.

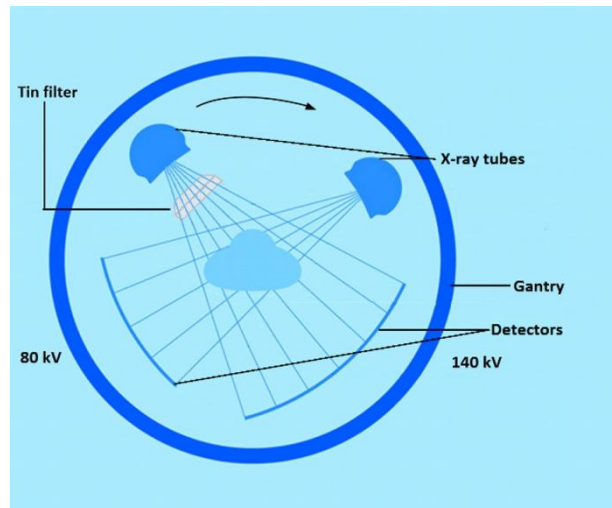


Figure 1 : Schematic image of Siemens SOMATOM Definition Flash DECT Scanner [17]

Table 2 : Technical Specifications of Siemens SOMATOM Definition Flash DECT [18]

Specifications	
Data Collection Diameter	500 mm
Distance Source to Detector	1085.6 mm
Distance Source to Patient	595 mm
The width of detector array	64 x 0.6 mm
Number of effective detector rows	2 x 64
Number of detector elements	47104 (A), 30720 (B)
Tube voltages	80, 100, 120, 140 kV

The larger detector (A) has 736 channels, the smaller detector (B) has 480 channels

2.3 Brachytherapy

Brachytherapy (BT) is a form of radiotherapy where one or more radiation sources are placed inside or close to the area requiring treatment [19]. It is commonly used as a treatment for breast cancer, prostate cancer, gynecological malignancies, skin cancer and tumors in different sites of the body. It uses sources emitting low energy photons typically between 20 keV and 400 keV.

BT treatment planning involves selecting catheter positions and source dwell times properly [20, 21] (in high dose rate (HDR) BT) or seed positions (in low dose rate (LDR) BT). Different dose calculation algorithms have been used. The approach currently used in commercially available treatment planning systems is the all water based dose calculation (TG-43) formalism [22]. Recently, image based dose calculation algorithms have been developed. The AAPM Task Group 186 (TG-186) [23] gives recommendations for the clinical implementation of these so called model based dose calculation algorithms (MBDCAs) including a review of the current status. Differences in calculated doses exceeding a factor of ten between MBDCAs and TG-43 formalism for specific BT cases have been reported [1]. According to TG-186 [23], it is therefore an urgent need to find methods for improved patient specific tissue classification.

2.4 ImageJ

ImageJ is an open source, Java based image processing program. It provides extensibility via Java plugins and macros. ImageJ supports displaying, editing, processing, analyzing and saving 8 bit, 16 bit and 32 bit images. It can read many image formats like JPEG, BMP, GIF, TIFF, DICOM etc [24]. In this work, ImageJ was used for the following tasks:

2.4.1 Preparation of a stack of sorted DICOM images

ImageJ supports use of stacks that are series of images shown in a single window. But it provides a limited support to work with DICOM files or create a sorted list of DICOM images. Sorted DICOM images can be prepared via the DICOM Sort.class plugin or DICOM_Sorter.txt macro. More information is in the documentation to this software packages.

2.4.2 Reading an exam series

Series of images can be read by using either the ‘File / Import / Stack From List...’ menu item or the TUDOR DICOM Manager. Before using the Import menu, the images should be split into series as described in Section 2.4.1. The DICOM Manager Tool makes it possible to read images for different exams and series defined in the DICOMDIR file. The DICOM Manager Toolbar is shown in Figure 2 and Figure 3.

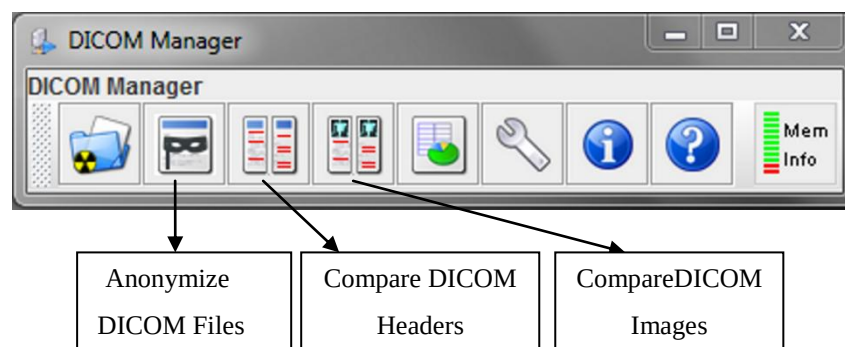


Figure 2 : Tudor DICOM Tools – Manager Window

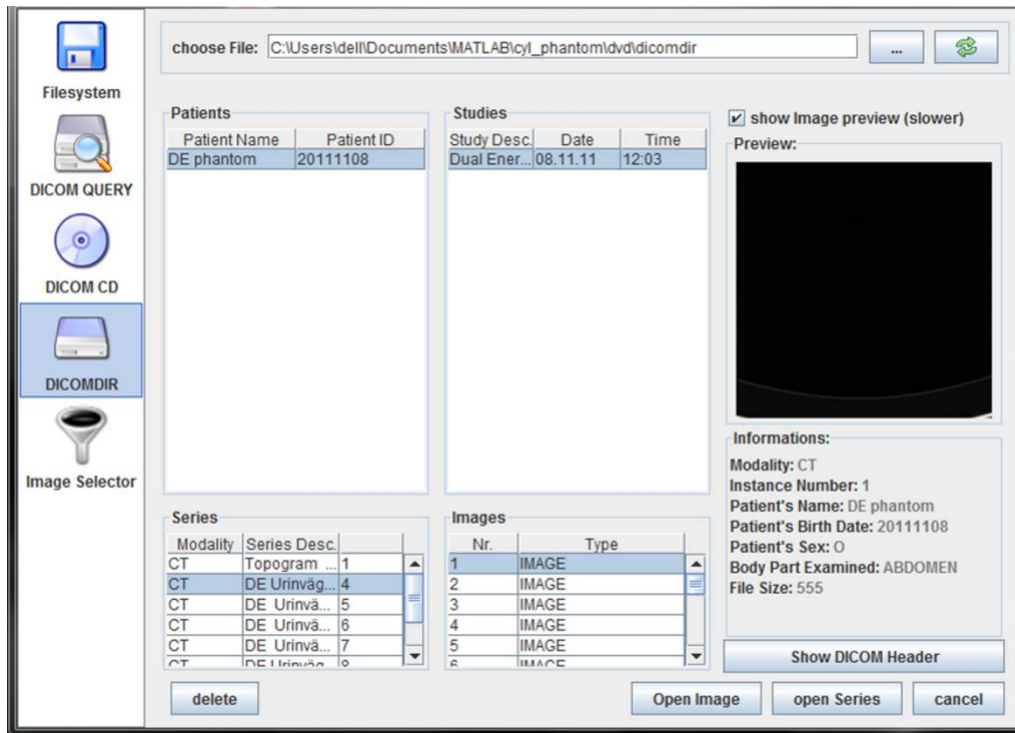


Figure 3 : Tudor DICOM Tools – Open Dialog

2.4.3 Working with regions and calculation of mean CT numbers

ImageJ can work with regions of interest (ROI) in the CT image. All types of region that are elliptical, rectangular, points or lines can be used. Selected regions can be organized in a ROI manager. The selected regions can be from different slices of a stack or different locations in the image. ROI manager shows the selected regions in the list window using names including slice number and x- and y-coordinates. The ROI manager can save the selected regions to a file with the .roi extension. This file can be loaded later. ROI Manager Tool and selected regions of cylindrical rod phantom are shown in the Figure 4.

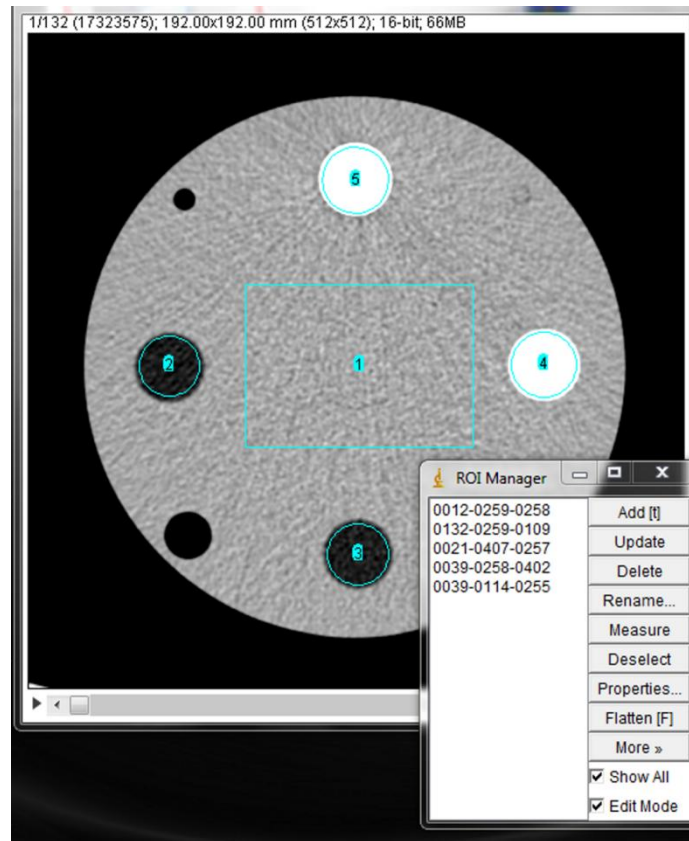


Figure 4 : ROI Manager and selected areas in the image

After regions of interest are determined, the ROI manager can perform statistical calculations like the calculations of mean values, standard deviations, areas of the regions, minimum and maximum values. Resulting values can be saved as a text file which can be read in MATLAB.

To select set of regions, following steps can be applied:

- 1) Zoom the image and select a window level so that the test tube wall is visible. The ‘CT Window Level’ plugin [25] allows for easy setting of contrast levels.
- 2) Determine first and last slices.
- 3) For a central slice, define a circular region (or a region of any shape) that is inside the wall of the test tube and does not contain air bubbles. Alternatively, eliminate air bubbles from further processing by selecting voxels that do not contain them.
- 4) Check that the region fits within the test tube walls for the first and last slices.
- 5) Add the region to the manager. Move the region to a new position using the keyboard and add it to the manager. Repeat the last step until all regions are added to the manager.

- 6) Show all regions and check that all regions are within test tube walls for all slices between the first slice and last slice.
- 7) Save the regions as a zip file using the ROI manager.

To process a set of regions, following steps can be applied:

- 1) Select 'Analyze / Set Measurements' menu item to set which statistics will be calculated. For instance, select 'Area', 'Standard Deviation' and 'Mean Gray Value'.
- 2) Select 'More / Multi Measure' menu item in the ROI manager to calculate the statistics.
- 3) Save the calculated values as a text file.

2.4.4 Profiles of CT numbers

ImageJ supports display of image profiles. A profile shows a graph of the intensities (gray values) of pixels along a line within the CT image. Figures 5.a-b show profiles of the cylindrical rod phantom obtained with the Sn140 kV spectrum. The figure 5a shows the profile of the cylindrical rod phantom along the x-axis and figure 5b shows the profile of the cylindrical rod phantom along the y-axis. In the graphs, the x-axis shows the distance (position) of the pixel along the line and the y-axis the pixel gray value.

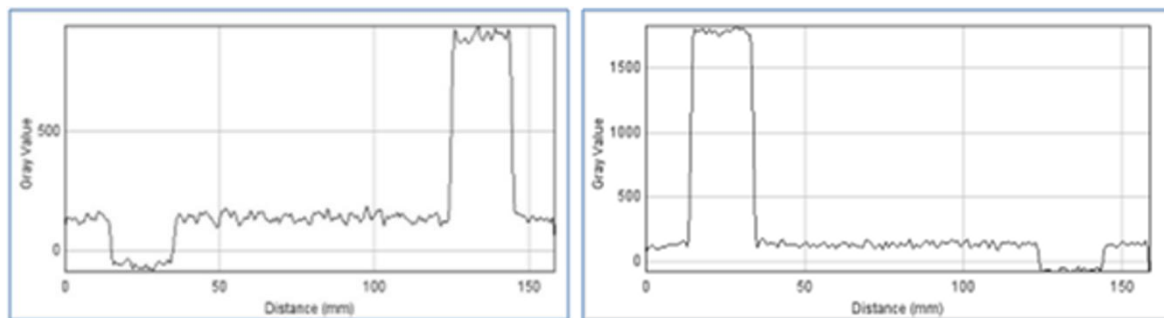


Figure 5 : Profiles for the cylindrical rod phantom at Sn140 kV a) along the x-axis b) along the y-axis

2.4.5 Histograms of CT numbers

ImageJ calculates and displays a histogram of the distribution of the gray values in the image or selected region of the image. Figure 6 shows a histogram based on values taken along a line (marked in yellow) in the image. The x-axis shows the gray values and the y-axis the number of pixels for each gray value.

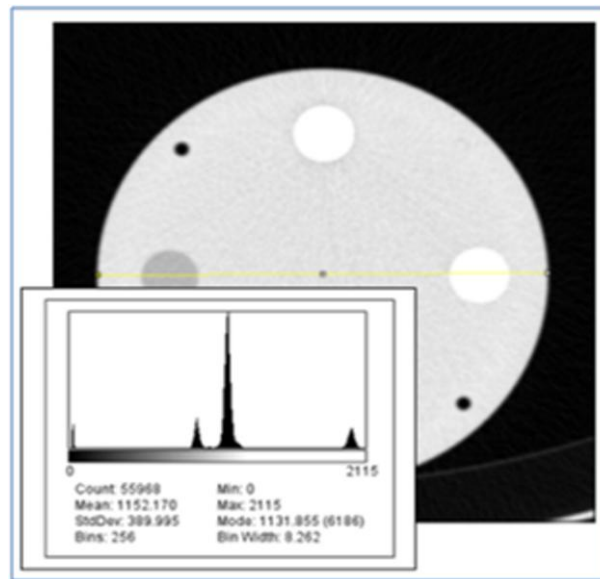


Figure 6 : Distribution of gray values for the pixels along the yellow line in the image

2.5 Statistics

The sample mean is defined as

$$\bar{x} = \frac{1}{N} \sum_{i=1}^N x_i \quad (2)$$

where N is the number of observations and x_i is the value of the observation i .

The sample standard deviation is defined as

$$s = \sqrt{\frac{1}{N-1} \sum_{i=1}^N (x_i - \bar{x})^2} \quad (3)$$

where $x_1, x_2, \dots, x_N$ are the observations, N is the number of the observations and $\bar{x}$ is the sample mean calculated from equation (2).

Standard deviation about the sample mean $\bar{x}$ can be calculated as

$$s_{\bar{x}} = \frac{s}{\sqrt{N}} \quad (4)$$

where N is the number of observations in the sample and s is the sample standard deviation calculated from equation (3). Equation (4) can be written as:

$$s_{\bar{x}} = \sqrt{\frac{1}{N(N-1)} \sum_{i=1}^N (x_i - \bar{x})^2} \quad (5)$$

For a region of interest selected in an image, ImageJ can calculate average pixel value from equation (2) and standard deviation from equation (3). ImageJ can calculate standard deviation and average pixel value for regions in one slice or in a stack of slices. Average pixel value and associated uncertainty for a volume region can be calculated from statistics provided by ImageJ as follows.

Volume average of pixel values in the selected slices in the image can be calculated as

$$\bar{x} = \frac{1}{N} \sum_{i=1}^N \bar{x}_i \quad (6)$$

where N is the number of slices in the volume and $\bar{x}_i$ is the average pixel value calculated from equation (2) for slice i .

To calculate uncertainty of the selected slices average (uncertainty of volume average value) following steps can be applied:

Following calculation (equation (7)) is the same as equation (4).

$$u(\bar{x}) = \sqrt{\frac{1}{NM(NM-1)} \sum_{i=1}^N \sum_{j=1}^M (x_{i,j} - \bar{x})^2} \quad (7)$$

where N is the number of slices in the selected volume and M is the number of the pixel in the selected region. i and j represent slice index and pixel index, respectively. $\bar{x}$ is the average value of the selected slices in the volume which is calculated from equation (6).

Equation (7) can be written as

$$u(\bar{x}) = \sqrt{\frac{1}{NM-1} \left[\frac{M-1}{M} \frac{1}{N} \sum_{i=1}^N s_i^2 + \frac{1}{N} \sum_{i=1}^N (\bar{x}_i - \bar{x})^2 \right]} \quad (8)$$

where N is the number of slices and M is the number of pixel in the region. Standard deviation s_i^2 and averages $\bar{x}_i$ are provided by ImageJ.

Equation (8) can be written as

$$u(\bar{x}) = \sqrt{\frac{1}{NM-1} \left[\frac{M-1}{M} \text{Avg}(s_i^2) + \frac{N}{N-1} \text{StdDev}^2(\bar{x}_i) \right]} \quad (9)$$

where $\text{Avg}(s_i^2)$ corresponds to average value of the slice variance estimates and $\text{StdDev}^2(\bar{x}_i)$ corresponds to variance estimate of the slice average value. Equation (9) can be used to calculate the uncertainty of the volume average of voxel values in MATLAB.

Standard uncertainty of the sum or difference of two random variables: Let A and B be uncorrelated random variables. The standard uncertainty u_C of a sum or difference of these two random variables can be calculated according to GUM [26] as

$$u_C = \sqrt{(u_A)^2 + (u_B)^2} \quad (10)$$

where u_A and u_B are the standard uncertainties of A and B respectively.

3 Studies

3.1 Study 1: Determination Effective Energy of Siemens SOMATOM Definition Flash DECT Scanner

3.1.1 Introduction

Effective energy can be defined to be the mono-energetic photon energy at which the linear attenuation coefficient of a material equals the linear attenuation coefficient in the poly-energetic beam. Tofts found in 1981 that the effective energy depends on the material being measured [27, 28]. The question is whether such conclusion is still valid for contemporary clinical CT scanners or whether a single photon energy can be used as the effective energy for all materials in a CT image.

There are different types of phantoms available with different tissue substitutes which can be used to determine CT numbers of the materials and effective energy of the scanner. The Division of Radiological Sciences at Linköping University has a cylindrical rod phantom. This phantom is made of clear plastic, polymethyl methacrylate (PMMA), also called acrylic glass or acrylic, and has a diameter of 16 cm. It consists of three equal cylindrical blocks that are glued together and contains 4 types of rod shaped inserts of diameter 2.1 cm : two LDPEs (Low-density polyethylene), aluminum, Teflon which is also called Polytetrafluoroethylene (PTFE). Figure 7 shows the top and side views of the phantom.

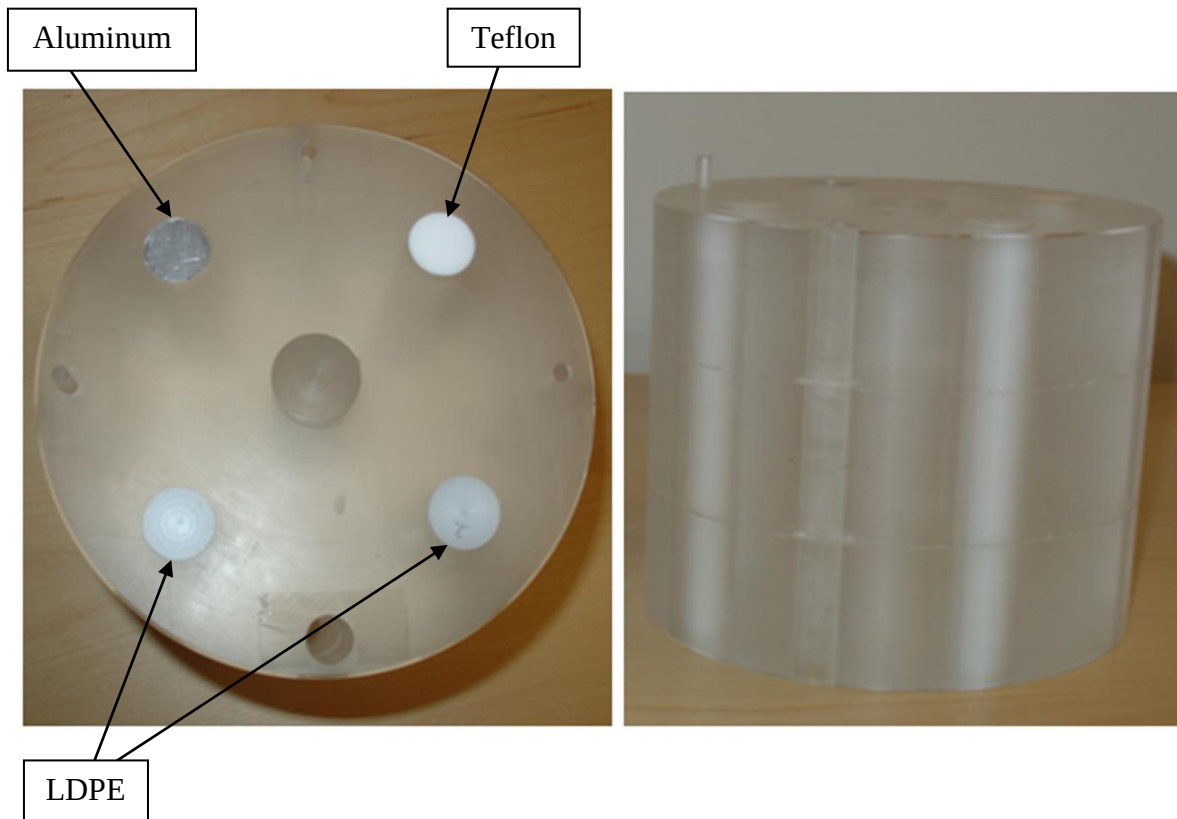


Figure 7 : The cylindrical rod phantom: Top view (left) Side view (right)

3.1.2 Aim

The aim of this study was to analyze data of the cylindrical rod phantom to get mean and standard deviations of CT numbers for voxels in well-defined regions and to determine effective energy of Siemens SOMATOM Definition Flash DECT Scanner for 80 kV and 140 kV with tin (Sn) filter (in the following described as Sn140 kV).

3.1.3 Method

The phantom was scanned by Siemens SOMATOM Definition Flash DECT using tube voltages 80 kV and Sn140 kV. Raw data were reconstructed using D30f reconstruction kernel which is a soft convolution kernel. The thickness of the slices was set to 1 mm.

Table 3 shows the properties of the materials in the phantom. Densities of LDPE1, LDPE2 and aluminum rods were calculated and densities of PMMA and Teflon were taken from [29, 30]. The acquired DICOM CT images were processed with ImageJ. A rectangular region of the PMMA and cylindrical regions of LDPEs, Teflon and aluminum were defined using the ROI Manager of ImageJ, see Figure 8. ROI manager provides calculation of mean CT number, standard deviation and area/number of pixels for each selected region. Results were

saved in a text file. These results were read and processed by MATLAB. For a detailed description of the process, see section 2.4.3.

Table 3 : Properties of the materials in the cylindrical rod phantom

Region	Material	Density (g / cm ³)	Estimated number of pixels in the region
R ₁	PMMA	1.18	1804.781
R ₂	LDPE1	0.928	177.750
R ₃	LDPE2	0.928	177.750
R ₄	Teflon	2.16	177.750
R ₅	Aluminum	2.691	177.750

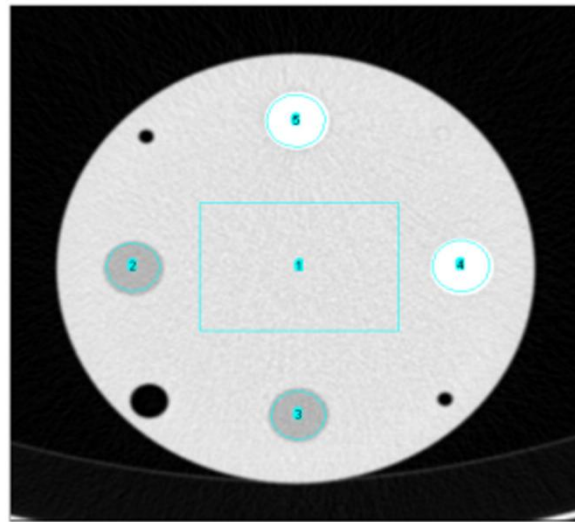


Figure 8 : Regions of interest for each material

PMMA (1), LDPE1 (2), LDPE2 (3), Teflon (4), Aluminum (5)

The effective energy of Siemens SOMATOM Definition Flash DECT Scanner was determined for the 80 kV and Sn140 kV spectra using the results for the CT numbers of PMMA, LDPEs, Teflon and aluminum inserts and theoretical calculations of the CT numbers using values of linear attenuation coefficients for the materials.

To calculate effective energy of the Siemens SOMATOM Definition Flash DECT scanner, firstly, linear attenuation coefficients for mono-energetic photons of the materials and water were calculated according to the formula:

$$\mu = (\sum_{Co} + \sum_{in} + \sum_{Ph}) * \rho \quad (11)$$

where ρ is the mass density of the material, $\sum_{Co}$, $\sum_{in}$ and $\sum_{Ph}$ are the mass attenuation coefficients (MACs) for coherent scattering, incoherent scattering and photoelectric effect, respectively. MACs were taken from Evaluated Photon Data Library (EPDL 1997 version) [31].

The CT number of a material for the different energies was calculated using the following formula:

$$H(E) = \frac{\mu(E) - \mu_w(E)}{\mu_w(E)} 1000 \quad (12)$$

where $\mu(E)$ is the linear attenuation coefficient of the material, $\mu_w(E)$ is the linear attenuation coefficient of water at photon energy E .

Figure 9 shows how the effective energy is obtained from the measured CT number. In Figure 9, the calculated CT numbers (in terms of Hounsfield units Equation (12)) are plotted as function of photon energy E . Using the measured CT number H_1 the energy E_1 is found that corresponds to H_1 . The effective energy is thus the energy of mono-energetic photons that has the same CT number as that measured, i.e. $E_1 = E_{eff}$.

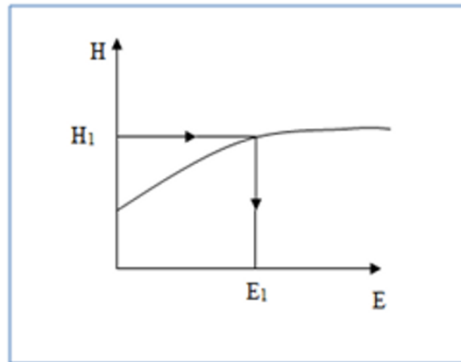


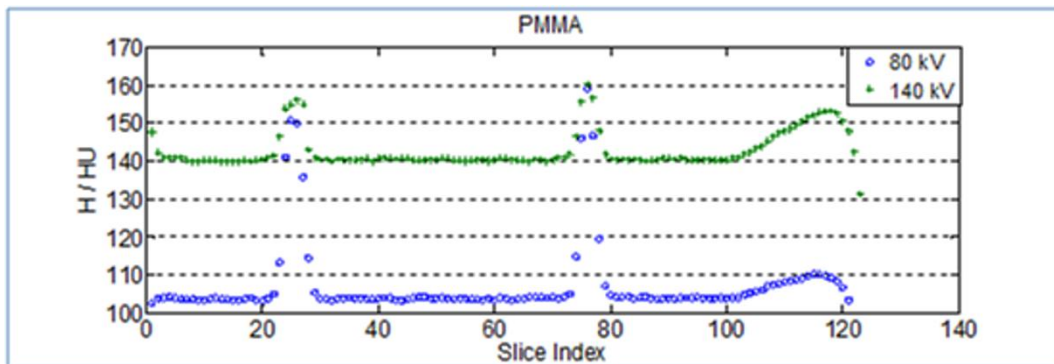
Figure 9 : Determination of effective energy. The curve shows the CT number (in Hounsfield units) as function of photon energy E calculated according to Equation (12). The photon energy E_1 corresponding to the measured CT number H_1 defines the effective energy E_{eff} ($E_1 = E_{ff}$)

3.1.4 Results and Discussions

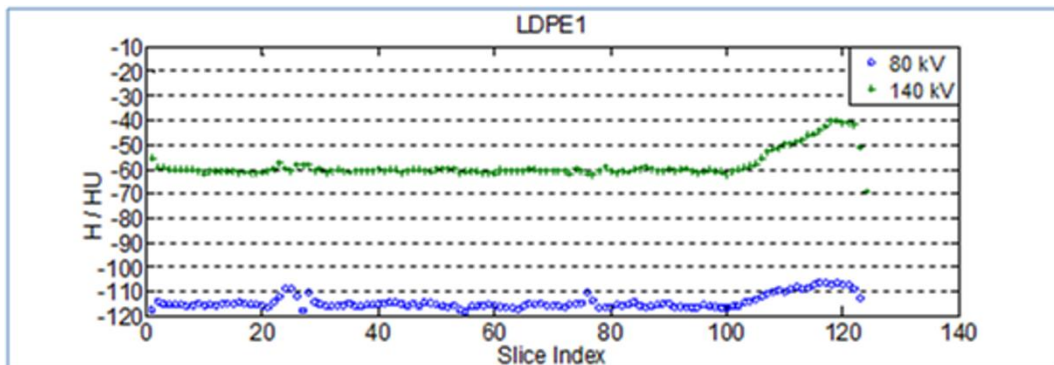
Average CT numbers in the regions of PMMA, LDPE, Teflon and aluminum as a function of slice index obtained with tube voltages 80 kV and Sn140 kV are shown in Figure 10.

As seen in Figure 10, there are up and down peaks for each material. Up peaks were clearly seen for the PMMA region. Down peaks were seen for aluminum and Teflon regions. These peaks were image artifacts caused by the glue between the cylindrical blocks.

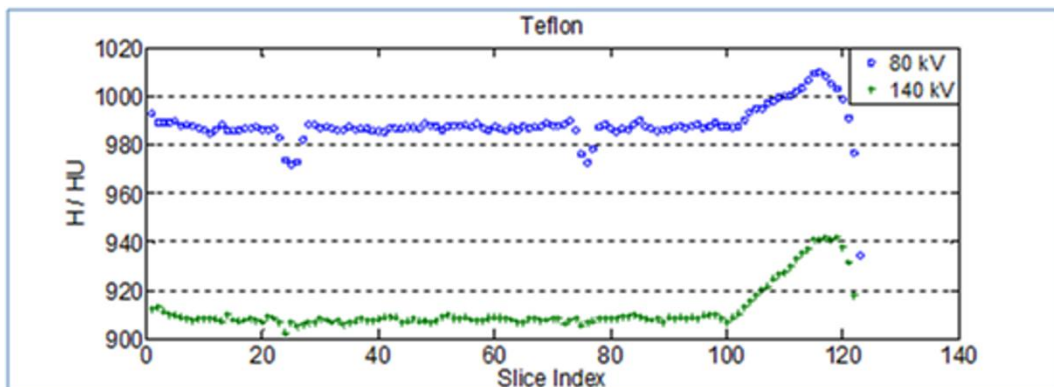
a)



b)



c)



d)

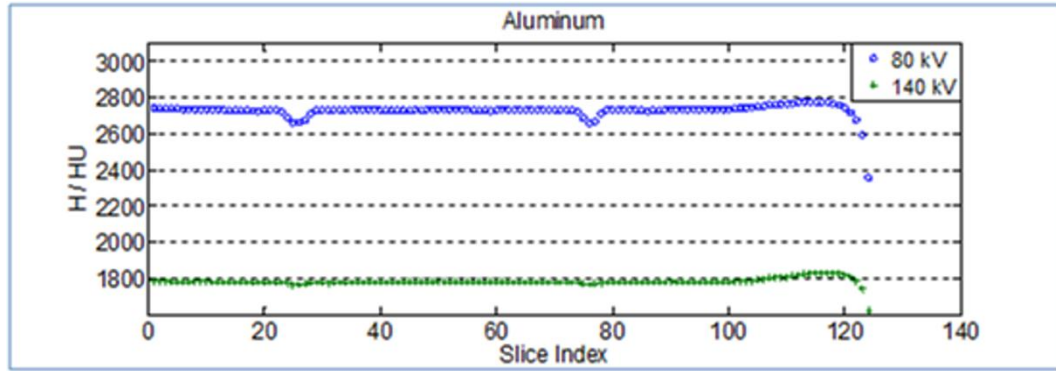


Figure 10 : Average CT number in regions of PMMA, LDPE, Teflon and aluminum as a function of slice index for 80 kV and Sn140 kV

The glue between the slices (seen as up and down peaks) restricted the region of interest. To find well defined regions in the plots, the CT numbers between two peaks (with slice index 30-70) were selected to calculate average CT numbers for all selected regions (for all the materials). The average CT numbers are shown in Table 4 with associated uncertainties. The uncertainties of the slices averages were calculated by Equation 9.

Figure 10a shows the average CT numbers for PMMA at the two different energies (tube voltages 80kV and Sn140 kV).

Figures 10c-d show the CT numbers of Teflon and aluminum. The measured CT number increased with increasing tube voltage for all materials except for Teflon and aluminum. This is due to, the fact that the linear attenuation coefficients of the aluminum and Teflon decrease more rapidly than the corresponding coefficient of water when the tube voltage increases from 80 kV to Sn140 kV.

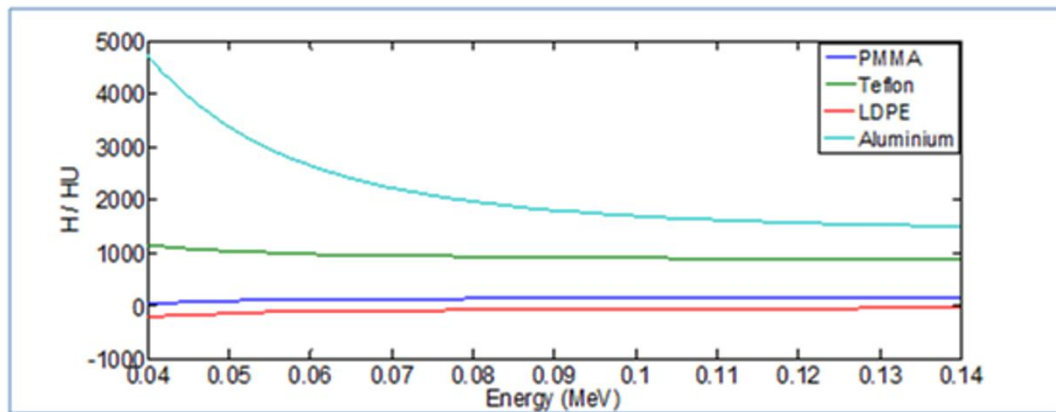
In Figure 10, it is moreover observed that CT numbers close to the last edge of the phantom increases which is probably caused by the image reconstruction kernel. The D30f kernel is a medium smooth (non-edge enhancing) kernel. This effect could be mitigated using a different kernel.

Table 4 : Average CT numbers of materials in the PMMA phantom

Material	80 kV	140 kV
PMMA	103.68 ± 0.03	140.24 ± 0.02
LPDE1	-115.64 ± 0.07	-60.76 ± 0.07
LPDE2	-114.29 ± 0.07	-59.06 ± 0.07
Teflon	987.12 ± 0.09	907.84 ± 0.08
Aluminum	2731.40 ± 0.19	1780.40 ± 0.09

Figures 11a-b shows the CT numbers of the materials as function of photon energy (calculated according to Eq (12)). The effective energies for the spectra were derived as described in Figure 9 using measured CT numbers from Table 4.

a)



b)

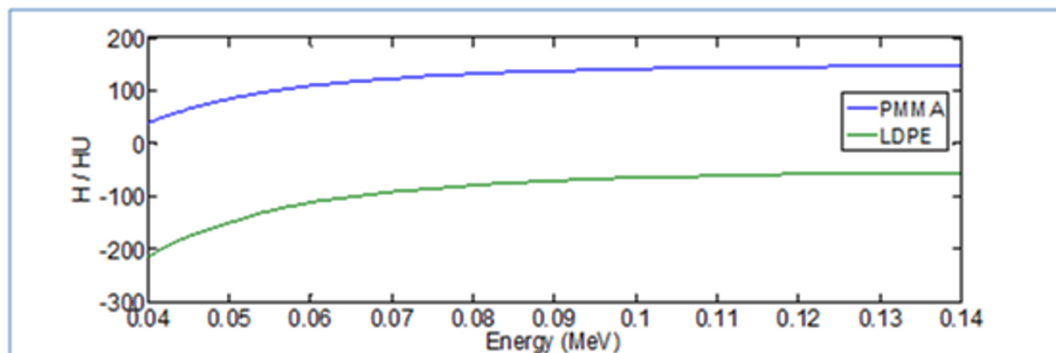
**Figure 11** : CT numbers as function of photon energy

Table 5 shows the effective energies with associated uncertainties for the 80 kV and Sn140 kV spectra. The uncertainties were calculated from equation 9.

Table 5 : Effective energies for the materials in the phantom at 80kV and Sn140 kV with uncertainties

Material	80 kV (keV)	Sn140 kV (keV)
PMMA	57.70 ± 0.01	100.80 ± 0.07
LDPE1	58.80 ± 0.02	112.80 ± 0.19
LDPE2	59.30 ± 0.02	119.20 ± 0.33
Teflon	57.00 ± 0.02	89.90 ± 0.06
Aluminum	58.30 ± 0.003	91.30 ± 0.007

3.1.5 Conclusions

The maximum relative difference among effective energies for 80 kV, was relatively small (less than 4%); and the average was (58 ± 1) keV. The effective energy of 58 keV was selected for subsequent measurements and calculations using the three material decomposition method. For Sn140 kV, the average (100 ± 13) keV was used. The maximum relative difference of 25% indicates that the image reconstruction algorithm resulted in different effective energies depending on the materials. In other words, the concept of a single effective energy is questionable for the Siemens' image reconstruction algorithm.

3.2 Study 2: Accuracy of CT Numbers

3.2.1 Introduction

Dual Energy CT (DECT) can theoretically be used for classifying tissues according to a three material decomposition scheme [32, 33, 34]. A requirement is that CT numbers are not affected by image artifacts such as beam hardening. To evaluate the accuracy of CT number measurements using the Siemens SOMATOM Definition Flash DECT scanner, a suitable phantom was designed. To estimate factors influencing the corresponding CT numbers four measurement tasks were proposed:

- 1) To observe differences in CT numbers of the test tubes using axial and helical scanning. The bottle is filled with air and the two different scanning modes are compared.
- 2) To observe how CT numbers are affected by the surrounding material, i.e., observe differences in CT numbers of the test tube when the bottle is filled with either air or water.
- 3) To observe how the CT numbers of test tubes are affected by a highly attenuating object in their neighborhood.
- 4) To check if CT numbers of water are 0 HU.

3.2.2 The test tube phantom: Materials and Methods Common to Task 1-3

The test tube phantom consisted of a plastic bottle and a test tube holder with 16 test tubes, see figure 12. The bottle had a volume of 15.4 L and was made of polyethylene. The holder (made of PMMA) consisted of two parallel plates connected with a central cylindrical tube. It contained 16 holes to hold the test tubes; eight of the test tubes were positioned in an inner circle with the radius of 4 cm, the other eight test tubes were positioned in an outer circle with the radius of 8 cm. The test tubes had an outer diameter of 17 mm, length of 110 mm and were made of polystyrene. The wall thickness of the tubes was 1 mm.



Figure 12 : Test tube phantom holder with 16 test tubes

The test tubes were filled with protein powder, crystalline salt, demineralized water and salt, sugar and protein solutions of varying concentrations, see Table 6. One of the test tubes with demineralized water was placed in the inner circle of the test tube holder and the other test tube with demineralized water was placed in the outer circle. Solutions were prepared in the chemistry laboratory of the Division of Radiological Sciences.

Table 6 : Mass fractions of materials used in the test tubes

Samples	w_i	
Salt Series	Water	Salt
B1 (salt crystals)		
B2	0.825	0.175
B3	0.875	0.125
B4	0.936	0.064
B5	0.978	0.020
B6 (demineralized water)	1.000	0.000
Protein Series	Water	Protein
B7	0.697	0.303
B8	0.787	0.213
B9	0.877	0.123
B10	0.963	0.037
B11 (protein powder)		
Sugar Series	Water	Sugar
B12	0.870	0.129
B13	0.909	0.091
B14	0.956	0.043
B15	0.988	0.012
B16 (demineralized water)	1.000	0.000

Configuration of the test tubes in the phantom is shown in Figure 13. This figure shows how the positions were labeled as regions for analysis in ImageJ. Table-7 shows the materials used in the test tubes. ‘Region’ column shows selected regions that are common for Task 1-3 in ImageJ.

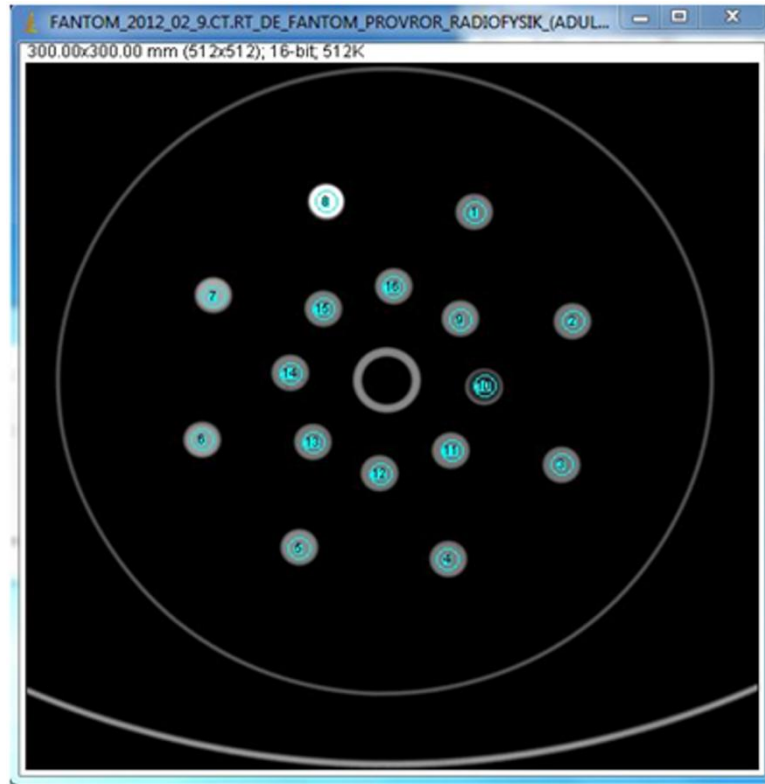


Figure 13 : CT scan of the test tube phantom taken at 80 kV. The bottle was filled with air and the test tubes were positioned according to the first column in Table 7.

Table 7 : Materials used in the test tubes and corresponding region labels in ImageJ. The symbol c_i denotes a concentration. c_1 stands for maximum concentration.

Region	Region*	Test Tube	Sample
R ₁	R ₃	B9	Protein+water (c_3)
R ₂	R ₄	B10	Protein+water (c_4)
R ₃	R ₅	B6	Demineralized water
R ₄	R ₆	B5	Salt+water (c_4)
R ₅	R ₇	B4	Salt+water (c_3)
R ₆	R ₈	B3	Salt+water (c_2)
R ₇	R ₁	B2	Salt+water (c_1)
R ₈	R ₂	B1	Salt crystals
R ₉	R ₁₁	B8	Protein+water (c_2)
R ₁₀	R ₁₂	B11	Protein powder
R ₁₁	R ₁₃	B16	Demineralized water
R ₁₂	R ₁₄	B15	Sugar+water (c_4)
R ₁₃	R ₁₅	B14	Sugar+water (c_3)
R ₁₄	R ₁₆	B13	Sugar+water (c_2)
R ₁₅	R ₉	B12	Sugar+water (c_1)
R ₁₆	R ₁₀	B7	Protein+water (c_1)

The average CT numbers with associated uncertainties and areas of selected regions were calculated using ImageJ according to Section 2.4.3.

To check that the selected regions did not include air bubbles, histograms of CT numbers were plotted. The test tubes were positioned as in the Region* (second) column in Table 7. For example, figure-14 shows the histograms for the configuration with the test bottle filled with water and the tube voltage of Sn140 kV. All distributions of CT numbers had approximately Gaussian shape except the one for regions R₂ and R₁₂ (test tubes B1 and B11 containing salt crystals and protein powder, respectively), (see section 3.2.4 for more information). Several outliers caused by air bubbles were observed for region R₁₁ (test tube B8 containing protein mixed with water). However, number of air bubbles was too small to effect resulting statistics.

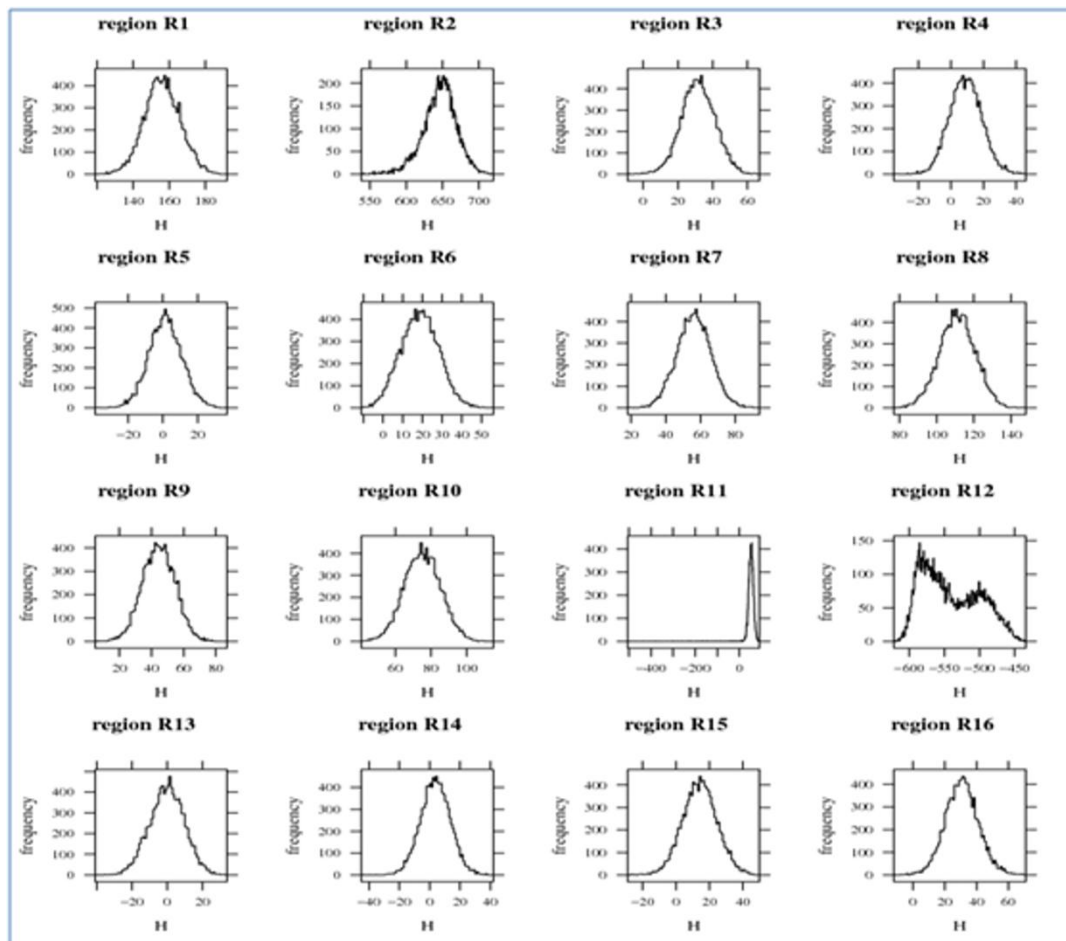


Figure 14 : Histograms of CT numbers for regions defined in ROI manager. Test tubes positioned in the regions are according to Table 7 second column (Region*). Histograms deviating from a normal distribution contain salt crystals (R₂), protein + water (c₂) (R₁₁) and protein powder (R₁₂)

3.2.3 Task 1: Comparison of Helical and Axial Scanning

Axial scanning is described as incremental scans with slice by slice imaging capability in which there is no table movement during the data acquisition. Helical scanning is described as a continuous scan; the table moves continually through the gantry when the tube rotates around the table and the patient [35].

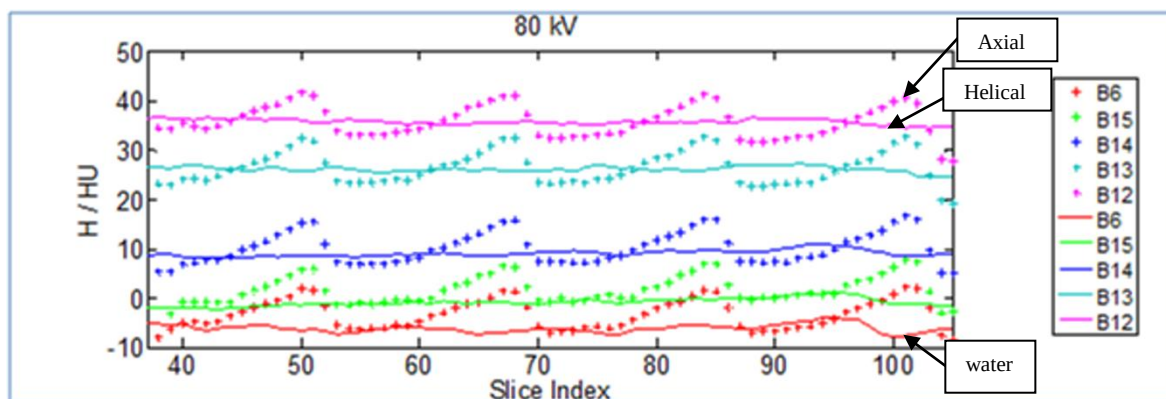
3.2.3.1 Methods

The test tube phantom was scanned using axial and helical scanning modes of the Siemens SOMATOM Definition Flash DECT scanner at 80 kV and Sn140 kV, the B31S reconstruction kernel and 1 mm slice thickness were used. The bottle was filled with air. Table 7 shows the test tube contents and positions of the test tubes (first column).

3.2.3.2 Results and Discussion

Figure 15 shows CT numbers for different concentrations of sugar solutions as a function of the slice number for both axial and helical scanning modes and for tube voltages of 80 kV and Sn140 kV. The distance between two maxima of the wave pattern was about 17 mm. This distance corresponds to the table shift between two data acquisitions in the axial scanning mode. The saw-tooth wave patterns were not observed in the helical scanning mode because the signal from the different detector rows were averaged in the helical mode.

Most likely, the saw-tooth wave patterns were caused by the heel effect of the x-ray tube which resulted in varying energy spectra at points across an x-ray beam in the anode to cathode direction due to the different absorption of x-ray photons in the anode target [36].



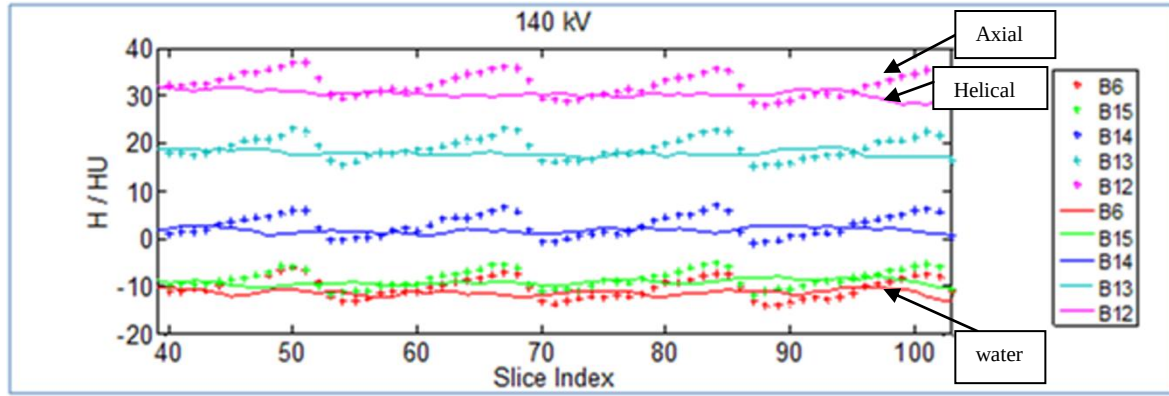


Figure 15 : The CT numbers of the water solutions of sugar at 80 kV and Sn140 kV.

Solid lines are for the helical mode and markers are for the axial mode

In Figure 15, the B6 test tube shows the CT numbers for water. The CT number for water was noticeably shifted from 0 HU being about -6 HU at 80 kV and -10 HU at Sn140 kV. In addition, these shifts depended on the type of reconstruction kernel used. Figure 16 shows profiles of the CT numbers using the reconstruction kernels B30s and B31s. The B30s kernel produced higher CT numbers than the B31s kernel and caused overshooting and undershooting at the edges.

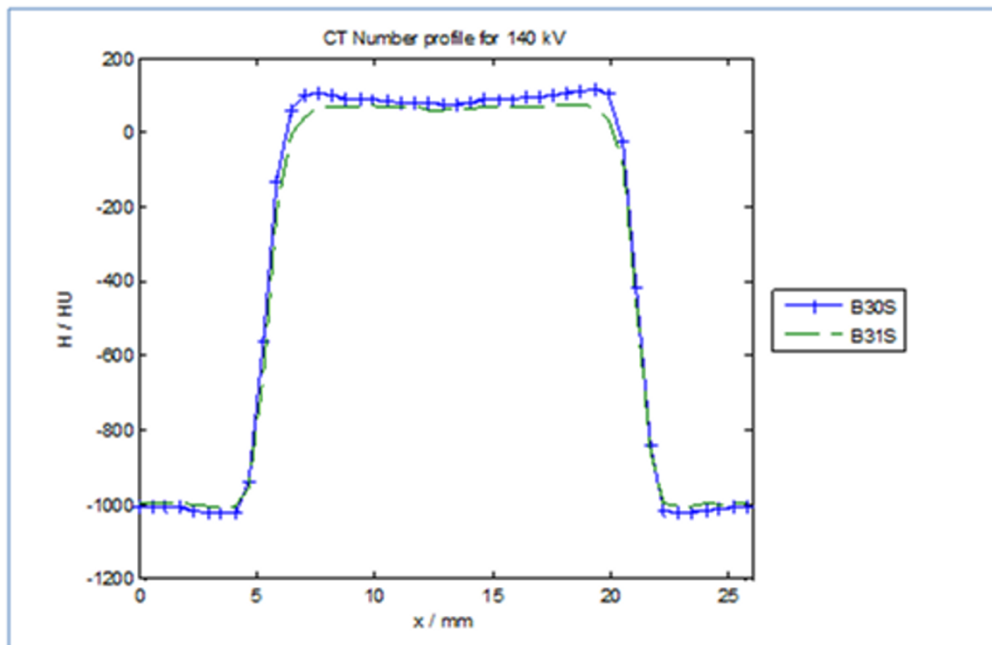


Figure 16 : CT number profiles of a test tube region for B30s and B31s reconstruction kernels using Sn140 kV.

3.2.4 Task 2: The effect of air filled bottle

3.2.4.1 Methods

The test tube phantom was scanned by Siemens SOMATOM Flash DECT Scanner using the tube voltages of 80 kV and Sn140 kV and with and without water in the phantom bottle. Table 7 shows the test tube contents and positions of the test tubes (first column).

3.2.4.2 Results and Discussion

Figure 17 shows the CT scans of the test tubes with and without water in the bottle. As seen in the figure, the noise of the image increased when the bottle was filled with water compared to the noise with only air in the bottle. This caused large uncertainties in the CT numbers obtained with the water filled bottle. The shift of the CT numbers was small when using the water filled bottle compared to the air filled bottle.

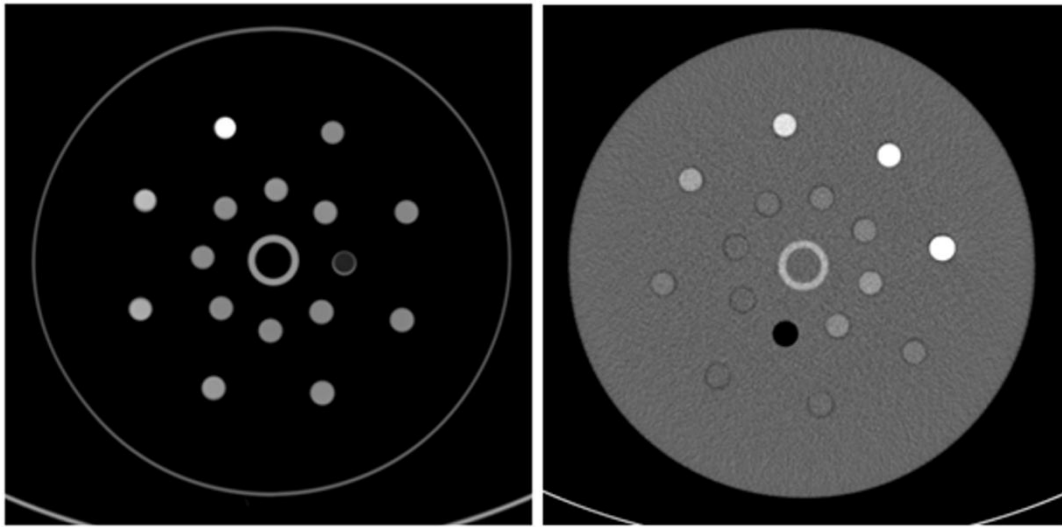


Figure 17 : CT scans of the test tube phantom with air (left) and water (right) in the surrounding bottle

Figure 18 shows the standard uncertainties associated with the average CT numbers for 80 kV and Sn140 kV. The uncertainties for the protein powder (tube B11) are relatively high because of spatial inhomogeneities of the protein powder inside the test tube; some parts of the protein powder were compressed more than others during the test tube filling, see the two peaks in the histogram for region R_{12} in figure 14. For salt, the standard uncertainties are relatively high most likely because of the partial volume effect which is responsible for slightly heavier left tail [37] of the histogram for region R_2 in figure 14.

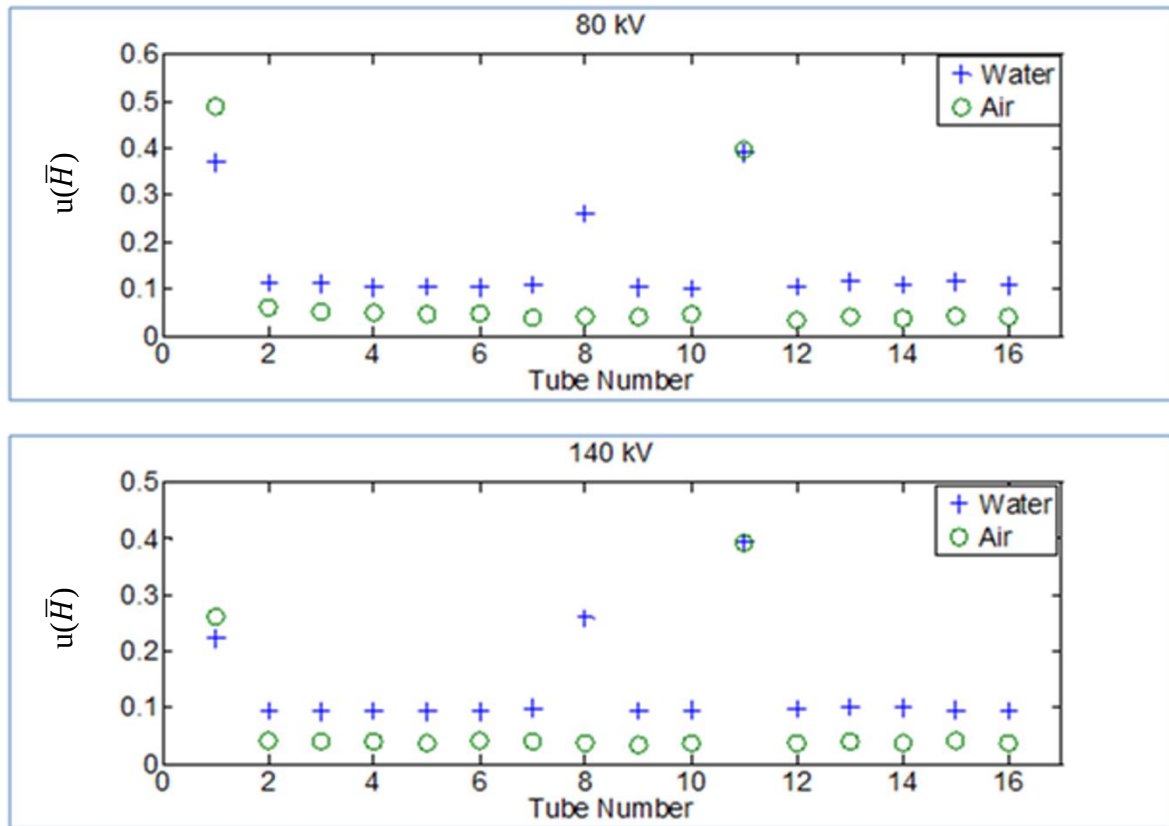
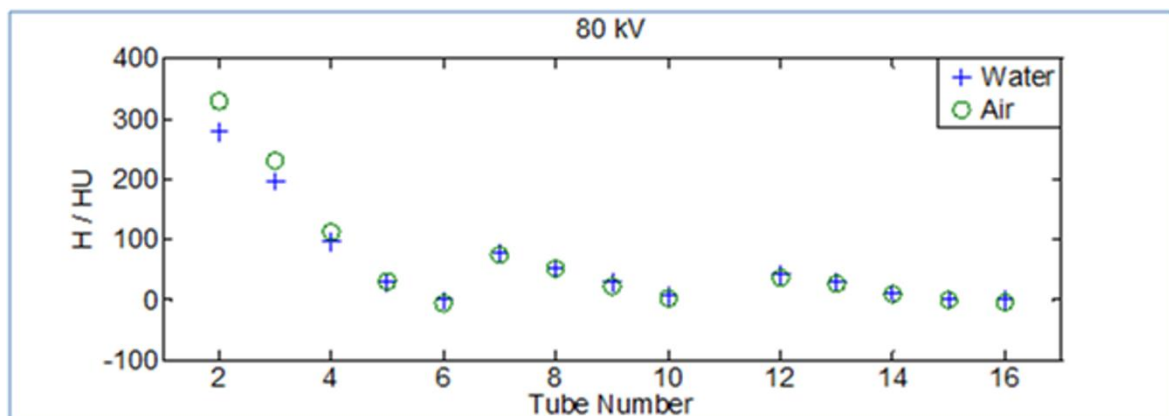


Figure 18 : Standard uncertainty about the mean CT number calculated from equation (8) for test tubes in two different surroundings; bottle filled with water (+) and with air (o). Tube voltage 80 kV (upper figure) and Sn140 kV (lower figure).

Figure 19 shows the average CT numbers for the test tubes B2-B16 except 11 (Table 7). The CT numbers were biased (shifted from true values) in the two different surroundings (bottle filled with air and with water), see Table 8. This shift of CT number was relatively large for Sn140 kV. The shift was small for 80 kV, the exception was the salt solutions (tubes B2, B3 and B4) where a crystallization of salt inside test tubes affected the measurement. (The samples were not properly homogenized before the CT scanning).



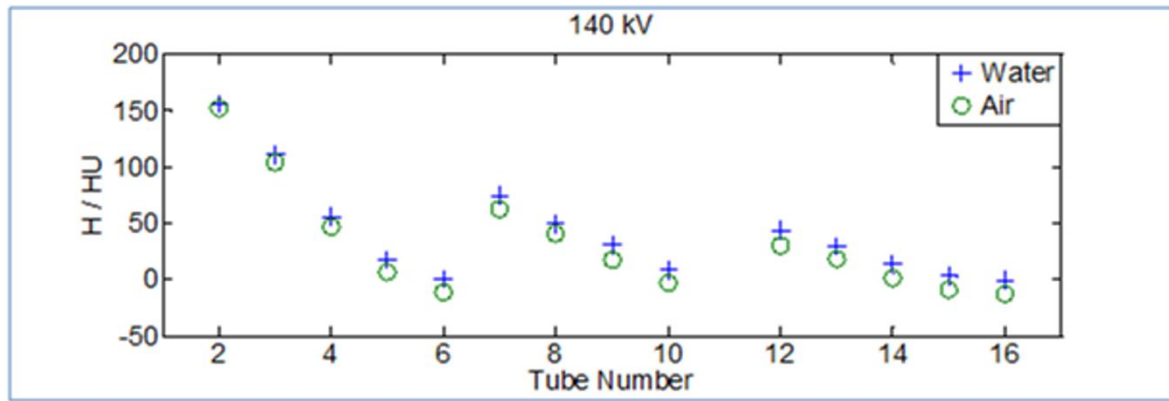


Figure 19 : Average CT numbers of the materials for different surroundings; bottle filled with water (+) and bottle filled with air (o).

Table 8 : Difference between average CT numbers with water and with air in the surrounding bottle for salt series (B1-B5) at 80 kV and at Sn140 kV (standard uncertainty of the difference was calculated from equation (10))

Samples	80 kV	140 kV
B1	236.01 ± 0.61	20.92 ± 0.34
B2	50.65 ± 0.12	3.08 ± 0.10
B3	34.35 ± 0.12	6.31 ± 0.10
B4	15.46 ± 0.11	8.66 ± 0.10
B5	1.05 ± 0.11	11.37 ± 0.09

3.2.5 Task 3: The effect of a highly attenuating object

3.2.5.1 Methods

The measurement was done with and without the test tube B1 that contained the highly attenuating salt crystals. The positions of the other test tubes were the same (first column in Table 7). The test tube phantom with the bottle filled with air was scanned by the Siemens SOMATOM Definition Flash DECT scanner at 80 kV and Sn140 kV.

3.2.5.2 Results and Discussion

Figure 20 shows the CT scan of the test tube phantom that includes Tube B1 and the neighboring test tubes (Tube B2, Tube B7, Tube B9 and Tube B12).

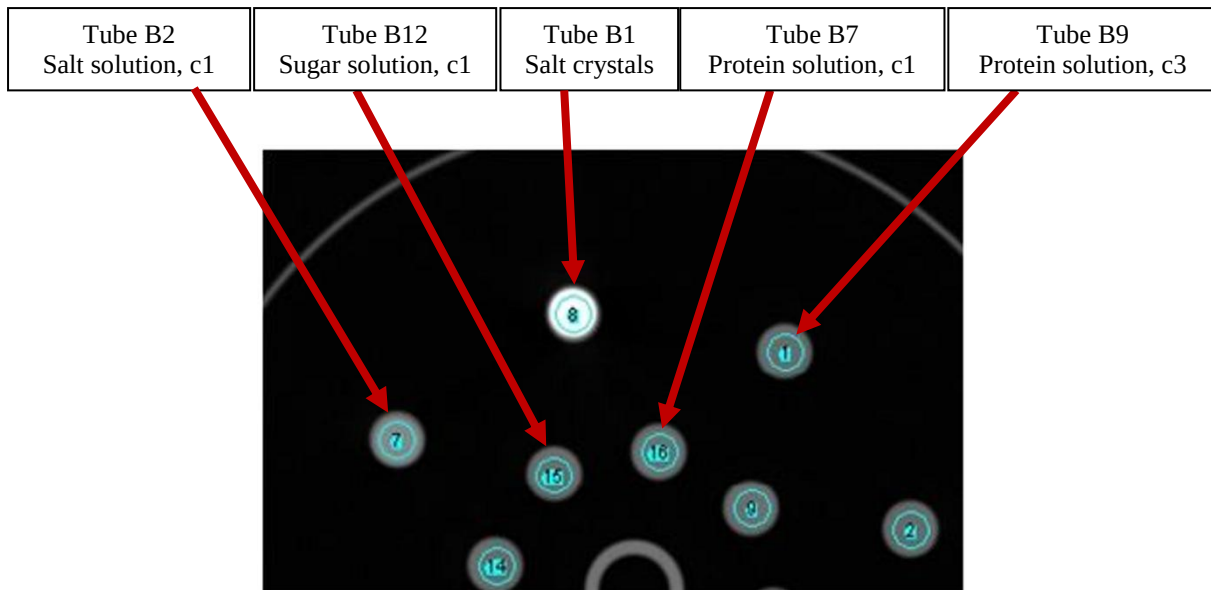
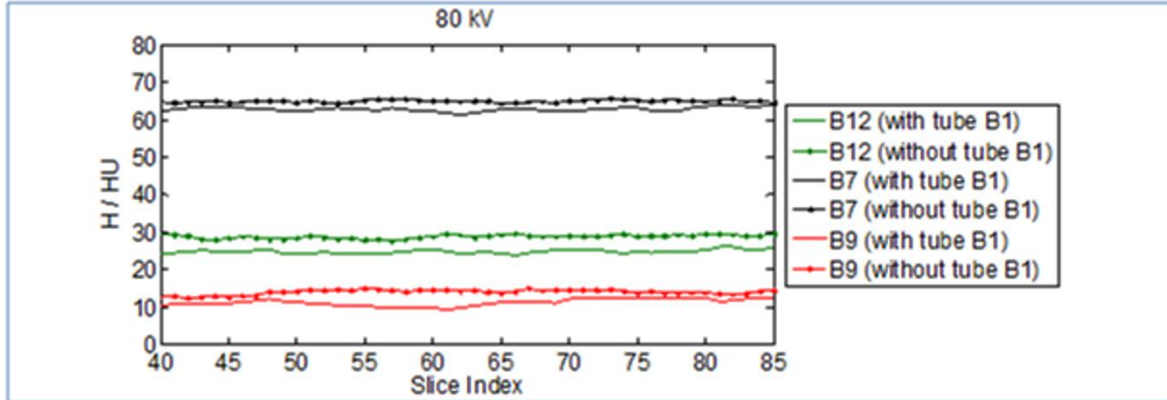


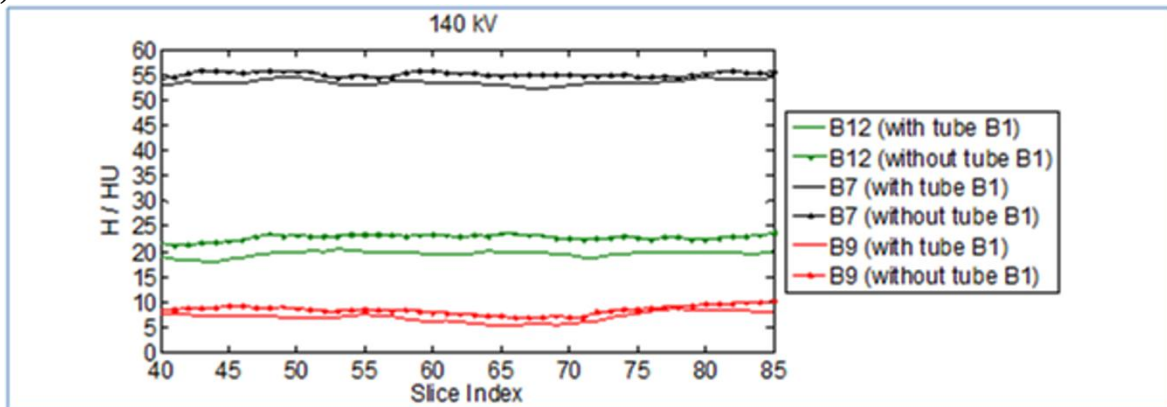
Figure 20 : CT scan of the test tube phantom with test tube B1 and neighboring test tubes.
Surrounding bottle was filled with air.

Figure 21a-b shows the shift of the CT numbers of the surrounding test tubes (B7, B9 and B12) and figure 21-c shows the shift of CT number of surrounding test tube B2 for 80 kV and Sn140 kV in the two different configurations (with and without test tube B1). The highly attenuating test tube (Tube B1) noticeably affected the CT numbers of neighboring test tubes only (test tubes B2, B7, B9, B12). The most likely explanation for this effect is beam hardening which caused the shift of CT numbers in neighboring tubes. The beam hardening can be explained as follows: An x-ray beam consists of individual photons with different energies. As the beam passes through the object (Tube B1), it becomes harder (the mean energy increases) as lower energy photons are absorbed more easily than the higher energy ones. This effect may lead to two types of artifact that are cupping artifacts and appearance of dark bands or streaks between two dense objects in the image.

a)



b)



c)

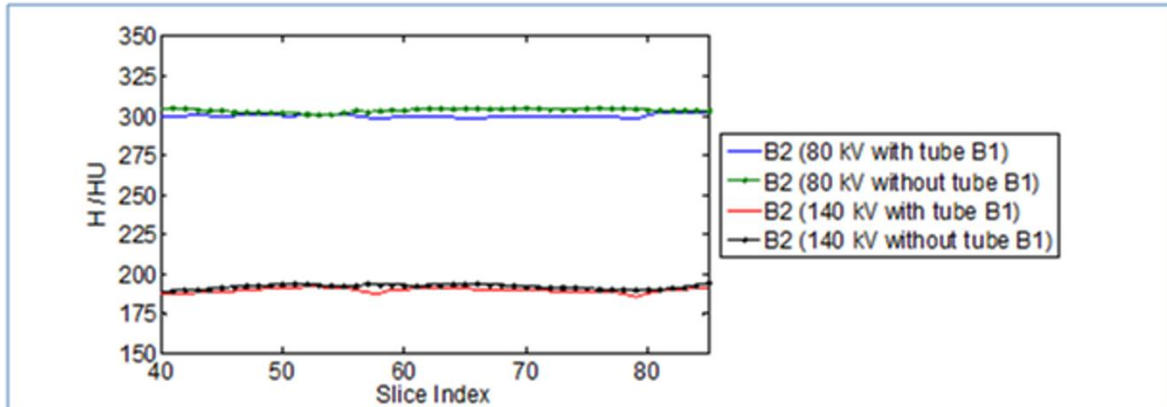


Figure 21 : The shift of CT numbers. **a)** Average CT numbers of surrounding test tubes (B7,B9,B12) for 80 kV in two different configurations (with and without tube B1). **b)** Average CT numbers of surrounding test tubes (B7,B9,B12) for Sn140 kV in two different configurations (with and without tube B1). **c)** Average CT number of surrounding test tube (B2) for 80 kV and Sn140 kV in two different configurations (with and without tube B1).

3.2.6 Task 4: The shift of CT numbers of demineralized water

3.2.6.1 Methods

All the test tubes were filled with demineralized water. The test tube phantom with bottle filled with air was scanned by Siemens SOMATOM Definition AS+ scanner using the tube voltages 80 kV and Sn140 kV. Test tubes with demineralized water positioned in the outer and inner circles of the test tube holder were labeled as $R_1, \dots, R_8$ and $R_9, \dots, R_{16}$ respectively.

3.2.6.2 Results

Figure 22 shows the average CT numbers and standard uncertainties with the average CT numbers (calculated from equation (8)) for water as a function of the region index obtained with tube voltages 80 kV and Sn140 kV. CT numbers for water were shifted away from zero to a degree depending on the position of the test tube, see figure 22. The largest shift was about -22 HU. This shift was most likely caused by the Siemens' beam hardening correction algorithm. The uncertainties of the test tubes are relatively higher for Sn140 kV than the uncertainties of the test tubes for 80 kV. In general, the uncertainties for the test tubes are low for both 80 kV and 140 kV.

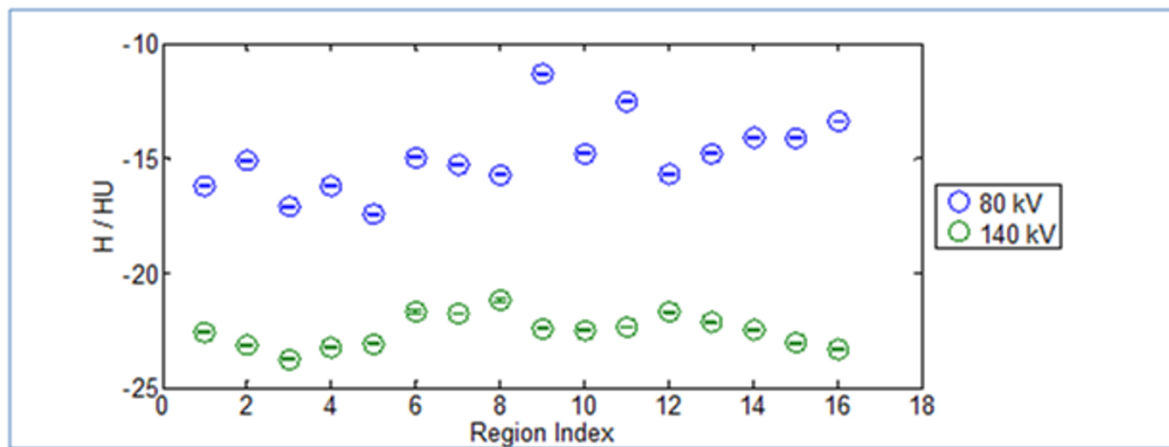


Figure 22 : The variations of the CT number for water measured on Siemens SOMATOM Flash AS+ scanner. Region index gives the position of the test tubes in the phantom.

Surrounding bottle filled with air.

3.2.7 Conclusions

This study was done to estimate the accuracy of CT numbers measured with clinical CT scanners. Firstly, axial scanning caused saw-tooth wave patterns. These patterns were averaged out when helical scanning was used. The author recommends use of helical scanning for quantitative CT measurements. Secondly, the air filled bottle biased measured CT numbers. For instance, the shift was up to -22 HU for water. The author recommends usage of water filled bottle even if it increases statistical noise as it lowers the intensity of the transmitted beam. Thirdly, reconstruction kernels affected the CT numbers, for instance compared to the B31s kernel the B30s kernel produced higher CT numbers in general and overshooting and undershooting at the edges. The author recommends usage of the B31s kernel for a three material decomposition. Fourthly, highly attenuating objects affected CT numbers of neighboring materials. The author recommends to take this effect into account in a three material decomposition method.

3.3 Study 3: Three Material Decomposition

3.3.1 Introduction

Dual energy CT can be used for a three material decomposition. Performance of three material decompositions can be evaluated by using a suitable phantom. The aim of this study was to evaluate the accuracy of the three material decomposition method when applied on mixtures scanned with the Siemens SOMATOM Definition Flash scanner.

3.3.2 Theory

3.3.2.1 N-Material Decomposition

To determine tissue composition, different approaches and methods can be used. One of these is the N-material tissue decomposition described below.

The N-material tissue decomposition method is based on the mixture rule also called the independent atom approximation (IAA) which assumes that an atom in the mixture is not affected by the presence of other atoms in the mixture. According to this, mass attenuation coefficient (MAC), μ/ρ , of a mixture of N individual components can be calculated as:

$$\mu/\rho = \sum_{i=1}^N w_i (\mu/\rho)_i \quad (13)$$

where $(\mu/\rho)_i$ is the MAC, w_i is the mass fraction of i th component, μ_i is the linear attenuation coefficient and ρ_i is the density. For M different photon energies $E_1, \dots, E_M$, equation (13) leads to a set of M equations:

$$\frac{\mu(E_1)}{\rho} = w_1 \frac{\mu_1(E_1)}{\rho_1} + w_2 \frac{\mu_2(E_1)}{\rho_2} + \dots + w_N \frac{\mu_N(E_1)}{\rho_N} \quad (14)$$

$$\frac{\mu(E_2)}{\rho} = w_1 \frac{\mu_1(E_2)}{\rho_1} + w_2 \frac{\mu_2(E_2)}{\rho_2} + \dots + w_N \frac{\mu_N(E_2)}{\rho_N} \quad (15)$$

...

$$\frac{\mu(E_M)}{\rho} = w_1 \frac{\mu_1(E_M)}{\rho_1} + w_2 \frac{\mu_2(E_M)}{\rho_2} + \dots + w_N \frac{\mu_N(E_M)}{\rho_N} \quad (16)$$

where w_i is the mass fraction for the component i . In this formula, the mass fractions $w_1, \dots, w_N$ are the unknown variables and the sum of all the mass fractions in the mixture equals 1:

$$1 = w_1 + w_2 + \dots + w_N \quad (17)$$

Mass density of a mixture, ρ , can be calculated as follows. Let m and V be the mass and volume, respectively, of a mixture, and let m_i , V_i and ρ_i be the same quantities for an i th component of the mixture. Suppose that the densities of each component, ρ_i , and mass fractions, $w_i = m_i/m$, are known parameters. If partial volumes of individual components are preserved when these components are added to the mixture, then the density of the mixture can be calculated as

$$\rho = \left(\frac{V}{m}\right)^{-1} = \left(\frac{1}{m} \sum_i V_i\right)^{-1} = \left(\sum_i \frac{m_i}{m} \frac{V_i}{m_i}\right)^{-1} = \left(\sum_i w_i \rho^{-1}\right)^{-1} \quad (18)$$

As mentioned before, Equation (18) requires that the volume of each component is preserved in the mixture. In this case, volume fractions of components can be transformed to mass fractions as

$$w_i = \frac{m_i}{m} = \frac{V_i \rho_i}{V \rho} = v_i \frac{\rho_i}{\rho} \quad (19)$$

The usage of mass attenuation coefficients is limited in CT since CT scanners measure linear attenuation coefficients. In case of CT, the mixture rule can also be used for linear attenuation coefficients (LAC), μ . The equation for a mixture of N individual components can be written as

$$\mu = \rho \sum_{i=1}^N w_i (\mu/\rho)_i = \frac{m}{V} \sum_{i=1}^N \frac{m_i}{m} \frac{\mu_i}{m_i/V_i} = \sum_{i=1}^N \frac{V_i}{V} \mu_i = \sum_{i=1}^N v_i \mu_i \quad (20)$$

where μ and μ_i are the LACs of the mixture and component i , respectively, m_i and V_i are the mass and partial volume of the i th component, respectively, m and V are the mass and volume of the mixture, respectively, and v_i is a volume fraction.

For M different photon energies $E_1, \dots, E_M$, equation (20) leads to a set of M equations and can be written as

$$\mu(E_1) = v_1\mu_1(E_1) + v_2\mu_2(E_1) + \dots + v_N\mu_N(E_1) \quad (21)$$

$$\mu(E_2) = v_1\mu_1(E_2) + v_2\mu_2(E_2) + \dots + v_N\mu_N(E_2) \quad (22)$$

...

$$\mu(E_M) = v_1\mu_1(E_M) + v_2\mu_2(E_M) + \dots + v_N\mu_N(E_M) \quad (23)$$

where μ and μ_i , $1 \leq i \leq N$, are the linear attenuation coefficients of the mixture and component i , respectively. In this case, sum of all the volume fractions (v_N) of the individual components equals 1.

$$1 = v_1 + v_2 + \dots + v_N \quad (24)$$

In equation (20), it is important to understand that m_i and V_i indicate the mass and partial volume, respectively, of the i th component both inside and outside the mixture. So that, the equation (20) requires that initial masses and partial volumes of individual components are preserved when these individual components are added to the mixture. If these conditions are fulfilled then equations (13) and (20) are equivalent and one equation can be transformed to the other equation. However, the partial volumes are generally not preserved in practice and for this reason, equations (13) and (20) may lead to different results.

Material decomposition can also be done from measured CT numbers. In this case, linear attenuation coefficients of the individual components are converted to CT numbers using the equation $H = (\mu/\mu_w - 1)1000$ where μ and μ_w are LACs of the material and water, respectively. In this case, equation (20) can be written as:

$$H = \sum_{i=1}^N v_i H_i \quad (25)$$

where H is the CT number of mixture and H_i are the CT numbers of the individual components of the mixture.

For M different photon energies $E_1, \dots, E_M$, equation (25) leads to a set of M equations and can be written as:

$$H(E_1) = v_1 H_1(E_1) + v_2 H_2(E_1) + \dots + v_N H_N(E_1) \quad (26)$$

$$H(E_2) = v_1 H_1(E_2) + v_2 H_2(E_2) + \dots + v_N H_N(E_2) \quad (27)$$

$$H(E_M) = v_1 H_1(E_M) + v_2 H_2(E_M) + \dots + v_N H_N(E_M) \quad (28)$$

where $H(E_i)$ is the CT number of the mixture for the i th photon energy and $H_i(E_j)$ is the CT number of the i th component for the j th photon energy. In this case, the sum of all the volume fractions (v_N) of the individual components equals 1.

$$1 = v_1 + v_2 + \dots + v_N \quad (29)$$

The CT numbers of the individual components and of the mixture can be measured by the CT scanner. The resulting system of equations can be used for determination of the volume fractions v_i .

3.3.2.2 Sample Preparation

This section describes how to calculate the mass of the 3rd component, m_3 , and mass of the mixture, m_{12} , of components 1 and 2 to obtain a mixture of components 1, 2 and 3 having mass fraction of the 3rd component equal to w_3 . It is supposed that the resulting volume is V_t and densities of the 3rd component and mixtures 1 and 2 are ρ_3 , ρ_m respectively.

In practice, the mass density of the mixture ρ_m can be calculated from equation (18) and can be written for mixture of two base materials as:

$$\frac{1}{\rho_m} = \frac{w_1}{\rho_1} + \frac{w_2}{\rho_2} \quad (30)$$

where ρ_1 and w_1 are the mass density and mass fraction, respectively, of the 1st base material and similarly for the symbols ρ_2 and w_2 corresponding to 2nd base material. To derive the unknown m_3 and m_{12} the following equations can be used:

$$V_t = V_3 + V_m = \frac{m_3}{\rho_3} + \frac{m_{12}}{\rho_m} \quad (31)$$

$$w_3 = \frac{m_3}{m_3 + m_{12}} \quad (32)$$

In equation (31), V_3 and V_m are the volumes of the 3rd component and mixture of the 1st and 2nd component, respectively. Equation (31) assumes preservation of partial volumes, which is not always the case. This system of equations can be written in a matrix notation as:

$$\begin{bmatrix} \frac{1}{\rho_3} & \frac{1}{\rho_m} \\ 1 - \frac{1}{w_3} & 1 \end{bmatrix} \begin{bmatrix} m_3 \\ m_{12} \end{bmatrix} = \begin{bmatrix} V_t \\ 0 \end{bmatrix} \quad (33)$$

or in a symbolic form as $Am = b$. Masses of the 3rd component and the mixture of two base materials may then be calculated as:

$$m = A b^{-1} \quad (34)$$

3.3.3 Materials and Methods

3.3.3.1 Preparation of Samples

In the experiment, demineralized water, gelatin, salt, protein and hydroxyapatite were used as components to prepare varying concentrations of mixtures. Demineralized water and gelatin and the 3rd component (salt, protein, hydroxyapatite) were mixed to prepare specific concentrations of the 3rd component. Calculation of recommended values is described in Section 3.3.2, and the values are presented in Table 9. Values used during the actual sample preparation are in Table 10.

During the experiment, masses of mixtures and individual components were measured with scales (Labassco HR-200 with the readability of 0.1mg, Sartorius BL 3100 with the readability of 0.1g). Gelatin and water were mixed in a beaker, heating and stirring were done using the Tamro Med-Lab RCT Basic KIKA-WERKE heater. For accurate measurement, the mass of the gelatin and water mixture was measured before and after heating. The amount of water that evaporated (about 0.436 g) was added after the heating to compensate for the loses; the evaporation rate was about 0.073 g / min. The 3rd component was added to the mixture of water and gelatin and the container was manually rotated until the gelatin solidified.

Table 9 : Calculated recommended masses of materials used in test tubes corresponding to various concentrations of the mixtures; the maximum concentration is labeled as cmax

Samples		Mass (g)	
Salt in gelatin + water	Water + Gelatin	Salt	
cmax 0.2	63.24	2.29	
cmax 0.4	62.13	4.67	
cmax 0.6	60.98	7.15	
Total sum	186.36	14.12	
Protein in gelatin + water	Water + Gelatin	Protein	
cmax 0.4	57.81	7.88	
cmax 0.7	52.75	14.02	
cmax	47.52	20.37	
Total sum	158.08	42.27	
Gelatin in water	Water	Gelatin	
cmax 0.25	62.87	1.94	
cmax 0.5	61.41	3.92	
cmax 0.75	59.93	5.93	
cmax	58.43	7.97	
Total sum	242.65	19.76	
HA in gelatin + water	Water + Gelatin	HA	
cmax 0.15	63.52	2.47	
cmax 0.3	62.69	5.08	
cmax 0.45	61.81	7.83	
cmax 0.6	60.89	10.74	
Total sum	248.91	26.14	

Table 10 : Measured masses of materials used in test tubes in physical experiments

Samples	Mass (g)	
Salt in gelatin + water	Gelatin + Water	Salt
D1	62.14	2.30
D2	61.83	4.69
D3	60.86	7.15
Total sum	187.076	14.14
Protein in gelatin + water	Gelatin + Water	Protein
D4	57.38	7.88
D5	52.41	14.05
D6	43.78	20.37
Total sum	158.59	42.3
HA in gelatin + water	Gelatin + Water	HA
D7	63.34	2.48
D8	62.75	5.09
D9	61.96	7.84
D10	59.83	10.76
Total sum	250.86	26.17
Gelatin in water	Gelatin + Water	Water
D11	16.06	48.63
D12	32.63	32.68
D13	49.36	16.48
D14	53.3	0
Total sum	164.7652	145
Water		Water
D15		53.3
D16		53.3

3.3.3.2 Reference mass fraction calculation

Masses of mixed components in Table 10 were used to calculate mass fractions of individual components as follows. Mass fraction of gelatin in the gelatin and water mixture was calculated as:

$$w_{gw} = \frac{m_{g,b}}{m_{g,b} + m_{w,b}} \quad (35)$$

where $m_{g,b}$ and $m_{w,b}$ are the masses of the gelatin and water, respectively in the large beaker with the gelatin-water mixture. Individual masses of gelatin and water in a sample container are then

$$\begin{aligned} m_g &= w_{gw} * m_{gw} \\ m_w &= m_{gw} - m_g \end{aligned} \quad (36)$$

where m_{gw} is the mass of the gelatin-water component. Mass fractions of the individual components were calculated as:

$$\begin{aligned} m_{tot} &= m_g + m_w + m_c \\ w_g &= m_g / m_{tot} \\ w_w &= m_w / m_{tot} \\ w_c &= m_c / m_{tot} \end{aligned} \quad (37)$$

where w_g , w_w and w_c are mass fractions of gelatin, water and the 3rd component, respectively, m_{tot} is the total mass of the mixture from Table 10.

3.3.3.3 Measurement of CT Numbers

Previous measurements (in Study 2) were affected from statistical noise and the usage of small test tubes were affected from reconstruction kernel that caused overshooting and undershooting at the edges. To eliminate these effects, a new phantom was designed using bigger containers. The phantom consisted of a plastic bottle and a phantom holder (made of PMMA) with 16 containers arranged in two levels. Each level contains eight containers whose centers are 7 cm from the main bottle axis, see figure 23. The bottle had a volume of 15.4 L and was made of polyethylene.

To evaluate the performance of the three material decomposition method, the phantom was scanned by Siemens SOMATOM Definition Flash DECT Scanner using tube voltages 80 kV and Sn140 kV. In this case, B31s kernel was used in the reconstruction. To determine average CT numbers of the mixtures for each test tube, firstly the regions of interest in the image were defined using ImageJ, see Figure 24. Figure 25 shows the schematic drawing of the test tubes for first and second levels. Coordinates of the selected regions are shown in Table 11. Secondly, histograms of the selected regions were plotted for 80 kV and Sn140 kV to show distributions of CT numbers for each voxel. Histograms for 80 kV and Sn140 kV are presented in Appendix. Thirdly, minimum and maximum CT numbers were determined for

each selected region for 80 kV. Voxels with CT numbers outside this range were excluded from processing. The selected voxels were used to calculate mean CT numbers and associated standard deviations for the selected regions. The calculated standard deviations were used to determine the new minimum and maximum values; the new range was selected as $\mu \pm 3\delta$. The resulting mean CT value was taken as the average from values in this new range.

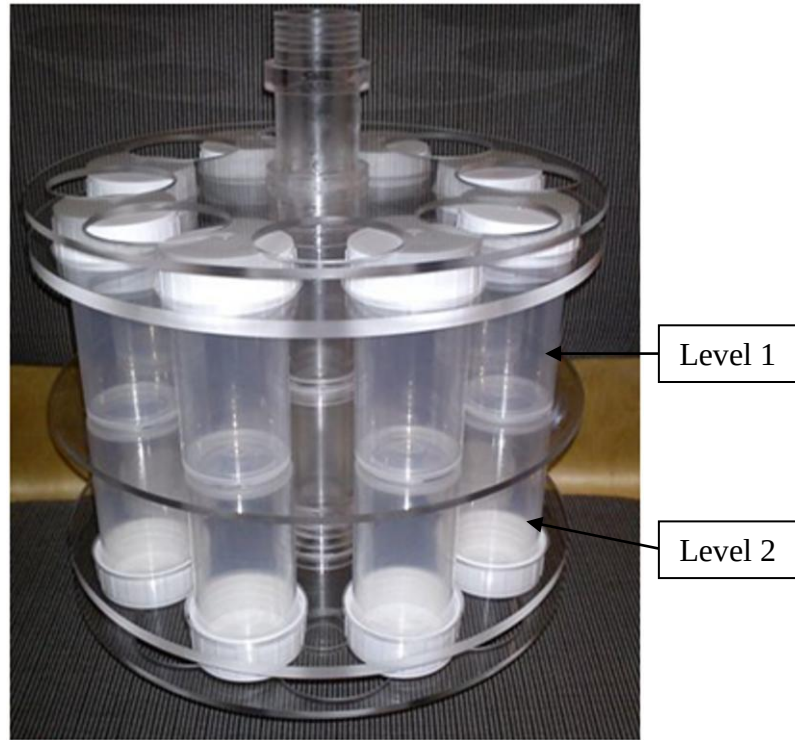


Figure 23 : The phantom holder with 16 containers

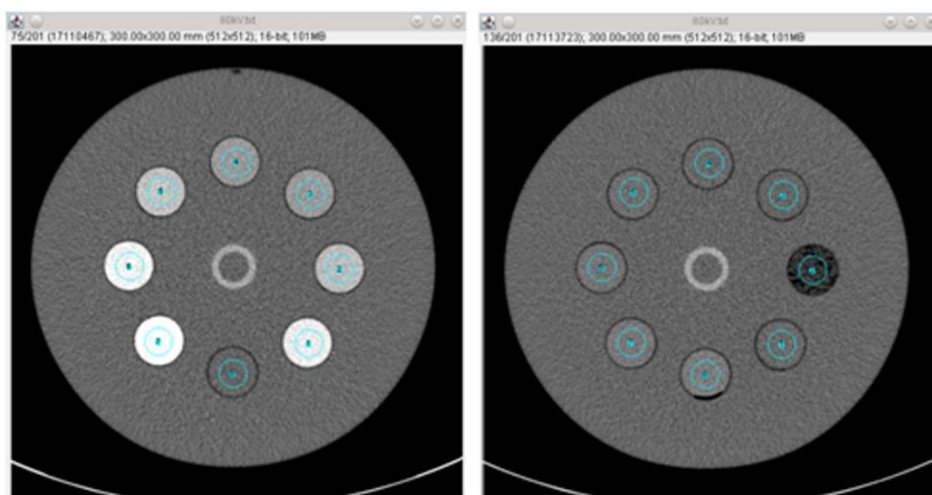
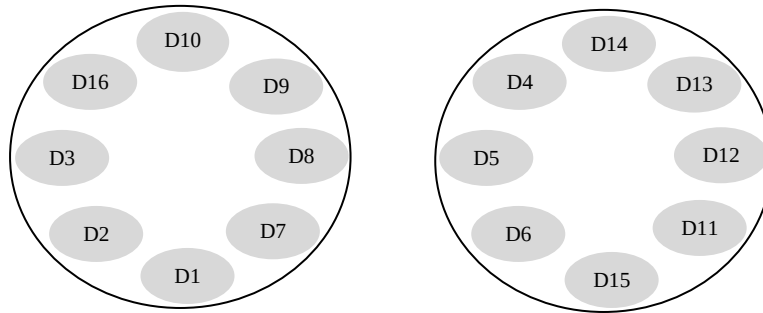


Figure 24 : CT scans of containers at level 1 (left) and level 2 (right) of the test tube phantom taken at 80 kV. The bottle was filled with water.

Table 11 : Coordinates of the selected regions in ImageJ

	Sample	Region	Center	Radius (mm)
Level 1	D10	7	97.559, 196.582	12
	D9	6	78.223, 146.777	12
	D8	5	99.316, 96.973	12
	D7	4	149.121, 77.637	12
	D1	3	198.340, 98.730	12
	D2	2	217.676, 148.535	12
	D3	1	197.168, 197.754	12
	D16	8	146.777, 217.676	12
Level 2	D14	7	97.559, 196.582	12
	D13	6	78.223, 146.777	12
	D12	5	99.316, 96.973	12
	D11	4	149.121, 77.637	12
	D15	3	198.340, 98.730	12
	D6	2	217.676, 148.535	12
	D5	1	197.168, 197.754	12
	D4	8	146.777, 217.676	12

**Figure 25** : Schematic drawing of positions of test tubes at level 1 (left) and level 2 (right)

3.3.3.4 Data Processing

This section describes the calculation of CT numbers of the individual components in the mixture. The CT number of gelatin was calculated from Equation (25) as

$$H_g = (H_m - v_w H_w) v_g^{-1} = H_m / v_g \quad (38)$$

where the symbols have the same meaning as in the section 3.3.2.1 and $H_w = 0$ HU. The subscripts g , w and m stand for gelatin, water and mixture, respectively. Volume fractions v_w and v_g were calculated from Equation (25), where the density of the mixture was calculated from Equation (18).

3.3.4 Results and Discussion

3.3.4.1 Reference mass fractions and calculated mass fractions using three material decomposition methods of components

In this section, resulting reference mass fractions was obtained from physical experiments (see section 3.3.3.2). Mass fractions calculated using the three material decomposition method referred to as H3 (see equation (19) and equation (25)) for different samples are presented. Table-12 compares mass fractions from experiments and mass fractions calculated using the three material decomposition method (H3) of each component for all mixture series. The agreement was good for the salt series (test tubes D1, D2 and D3) and HA series (test tubes D7, D8, D9 and D10). The maximum relative percentage differences where 8% and 15% for the salt and HA series, respectively. On the other hand, for the protein series (test tubes D4, D5 and D6), some H3 mass fractions were negative. This fact was most likely caused by the presence of very small air bubbles in the protein solutions. The air bubbles were trapped in protein powder and did not have enough time to escape before the gelatin solidified. The additional air lowered the CT number of the protein, water and gelatin mixture, and thus led to the observed discrepancy in mass fractions.

Table 12 : Reference and H3 mass fractions of water, gelatin and 3rd component

Samples		Reference (w_i)			H3 (w_i)		
Salt series	Water	Gelatin	Salt	Water	Gelatin	Salt	
D1	0.849±0.001	0.115±0.001	0.036±0.001	0.831	0.137	0.037	
D2	0.818±0.001	0.111±0.001	0.071±0.001	0.779	0.162	0.069	
D3	0.788±0.001	0.107±0.001	0.105±0.001	0.716	0.192	0.114	
Protein series	Water	Gelatin	Protein	Water	Gelatin	Protein	
D4	0.774±0.001	0.105±0.001	0.121±0.001	-0.384	-1.688	3.276	
D5	0.694±0.001	0.094±0.001	0.211±0.001	0.636	-0.383	0.745	
D6	0.601±0.001	0.082±0.001	0.318±0.001	4.277	4.272	-8.238	
HA series	Water	Gelatin	HA	Water	Gelatin	HA	
D7	0.848±0.001	0.115±0.001	0.038±0.001	0.852	0.113	0.030	
D8	0.815±0.001	0.110±0.001	0.076±0.001	0.804	0.130	0.061	
D9	0.782±0.001	0.106±0.001	0.112±0.001	0.754	0.147	0.097	
D10	0.747±0.001	0.101±0.001	0.152±0.001	0.696	0.174	0.130	
Gelatin series	Water	Gelatin					
D11	0.976±0.001	0.024±0.001	0.000				
D12	0.958±0.001	0.042±0.001	0.000				
D13	0.946±0.001	0.054±0.001	0.000				
D14	0.880±0.001	0.120±0.001	0.000				
Water							
D15	1.000	0.000	0.000				
D16	1.000	0.000	0.000				

3.3.4.2 Measured CT numbers

This section presents CT number diagrams calculated using the three material decomposition method according to section 3.3.3.4. Figure 26 and 27 shows CT number diagrams for each series (salt, protein and HA). The green triangle displays CT numbers of base materials in the mixture that were calculated from photon cross section data in the EPDL97 data library for photon energies of $E_1 = 58$ keV and $E_2 = 100$ keV. Red circles show the average CT number of the mixture for 80 kV and Sn140 kV.

For salt (test tubes D1, D2 and D3) and HA series (test tubes D7, D8, D9 and D10) most of the CT numbers are inside the base material triangle. On the other hand, most of the CT numbers for the protein series (test tubes D4, D5 and D6) are outside the triangle. In this case, the triangle is very flat because CT numbers of gelatin and protein have approximately the same values. It is clearly seen that a decomposition to protein, gelatin and water is problematic.

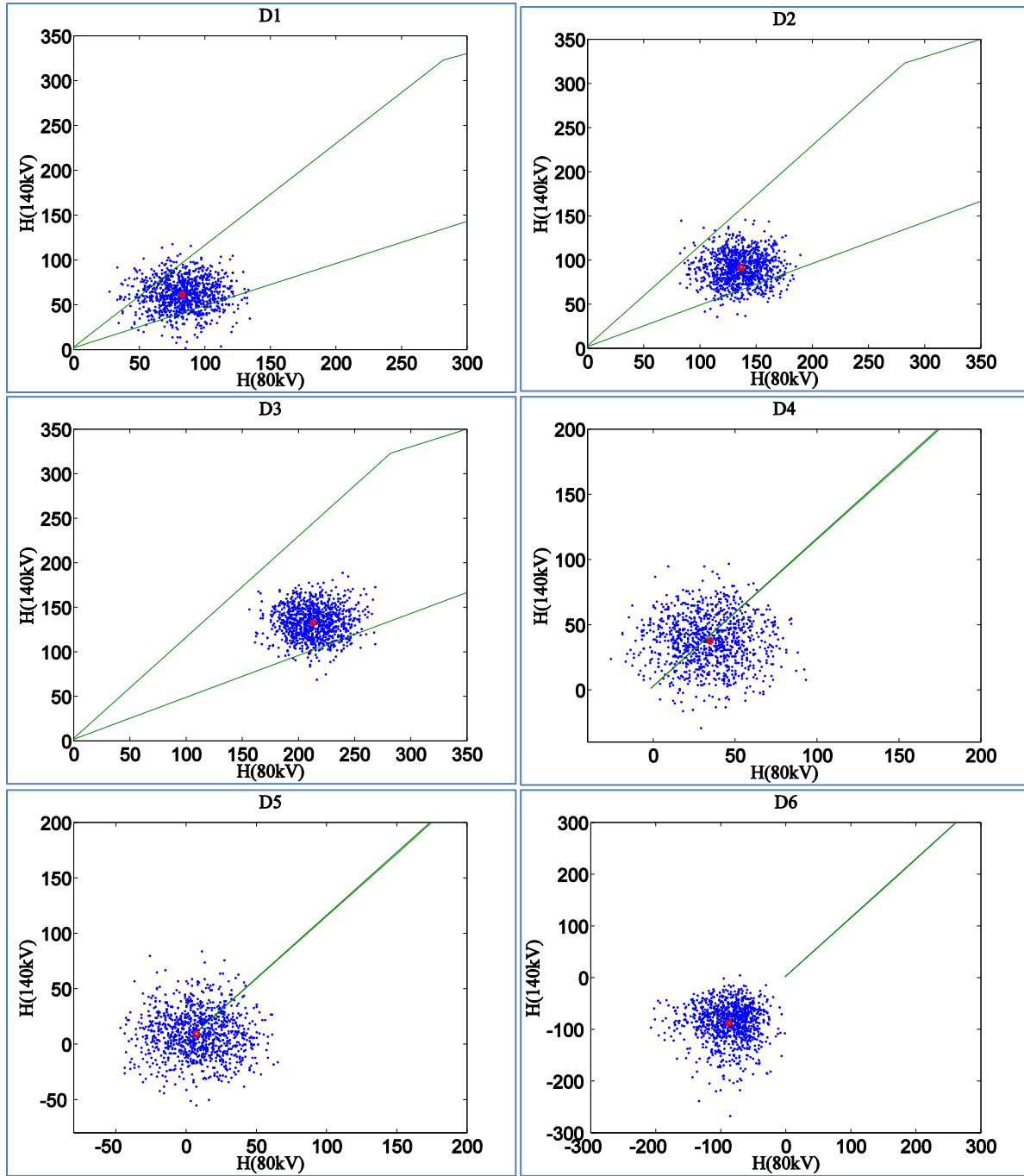


Figure 26 : CT number diagrams for three material decomposition for salt series (D1,D2,D3) and protein series (D4,D5,D6). The green triangle shows base materials. Red circles show average CT numbers of the mixtures for 80 kV and Sn140 kV.

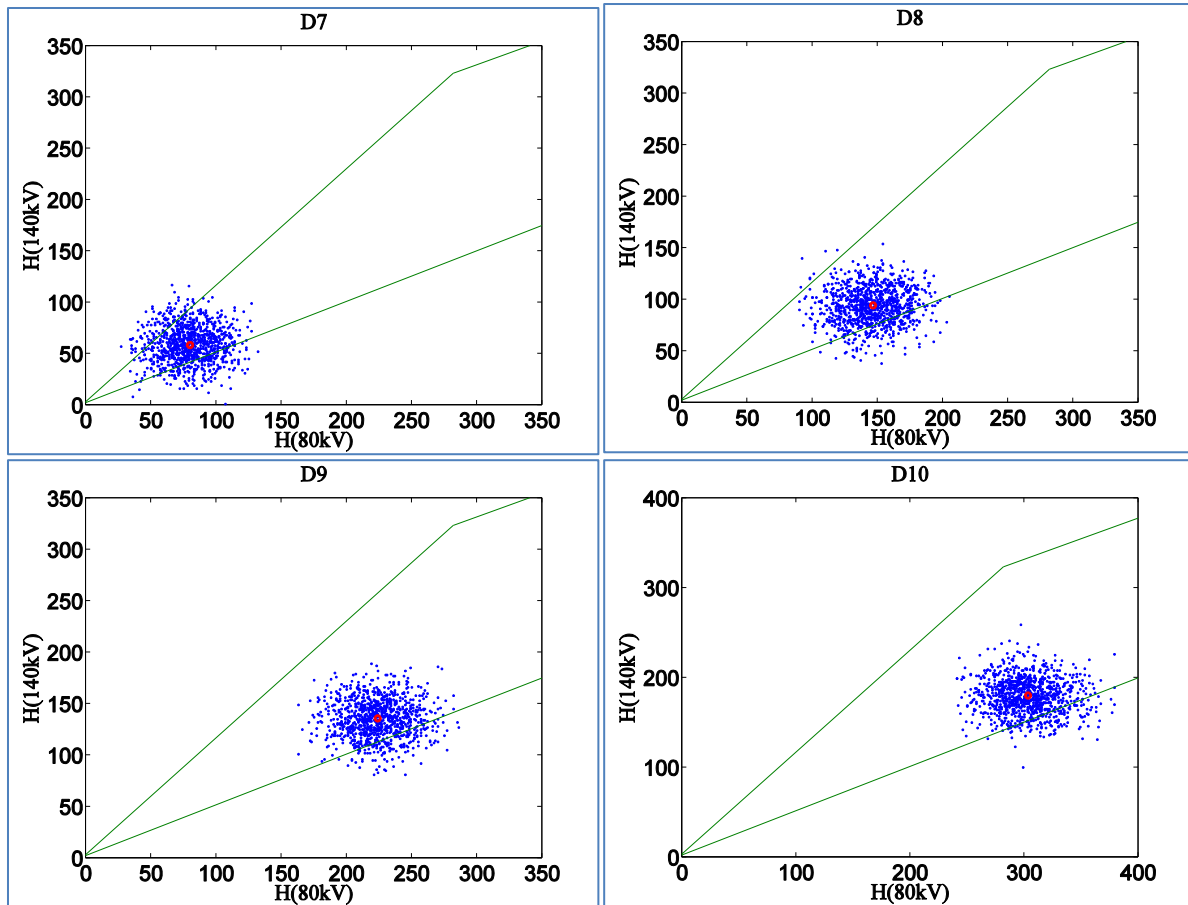


Figure 27 : CT number diagrams for three material decomposition for HA series (D7,D8,D9,D10)

Table 13 shows the minimum and maximum CT numbers which define the ranges that were used to determine averages and standard deviations for histograms presented in the Appendix according to the method in section 3.3.3.3. The number of voxels, N , for a selected region was used to calculate standard deviations about the mean values according to section 2.5. The negative CT numbers of water were within the limit of acceptance for CT numbers of water (± 4 HU).

Table 13 : Minimum, maximum and average CT numbers for 80 kV and Sn140 kV for each sample

Sample	Hmin	Hmax	$\bar{H}_{80}$	$\bar{H}_{140}$	N of voxels
Salt in gelatin					
D1	26	139	82.46 ± 0.09	62.12 ± 0.09	40970
D2	78	194	136.09 ± 0.09	91.75 ± 0.09	40989
D3	153	272	212.67 ± 0.09	133.12 ± 0.09	40989
Protein in gelatin					
D4	-27	96	34.56 ± 0.08	37.87 ± 0.08	54649
D5	-58	72	7.07 ± 0.09	9.92 ± 0.09	54617
D6	-212	29	-88.68 ± 0.15	-86.82 ± 0.15	53627
HA in gelatin					
D7	23	137	79.87 ± 0.09	58.48 ± 0.09	40957
D8	85	208	146.42 ± 0.10	94.36 ± 0.09	40979
D9	159	289	223.72 ± 0.10	135.90 ± 0.09	40953
D10	228	379	303.23 ± 0.12	180.20 ± 0.10	40651
Gelatin in water					
D11	-49	60	5.69 ± 0.08	8.00 ± 0.07	54635
D12	-41	67	12.89 ± 0.07	16.03 ± 0.07	54639
D13	-35	75	20.08 ± 0.08	24.06 ± 0.07	54654
D14	-29	84	27.54 ± 0.08	31.54 ± 0.07	54647
Water					
D15	-55	52	-1.45 ± 0.07	1.22 ± 0.07	54632
D16	-59	56	-1.48 ± 0.09	0.51 ± 0.09	40973

3.3.4.3 H3 volume fractions

In this section, ternary diagrams of resulting volume fractions of the base materials (Figure 28 and 29) and resulting volume fractions (Table 14) obtained from three material decomposition method (see Equation (26)) for different samples are presented.

Ternary diagrams were used to show volume fractions of the three base materials. Ternary diagrams can be interpreted as follows. 100% volume fractions correspond to vertices in the equilateral triangle. Each vertex in the triangle represents one base material. The volume fraction is the distance between the given point and the base opposite to the vertex relative to the height of the triangle. When the point is outside the triangle the distance from the base should be taken as negative.

Points outside the triangle (negative volume fractions) were observed for each sample. The points were located inside elliptical regions. The flatness of the ellipse indicates correlation

between volume fractions. For the protein series, the elliptical regions were very flat and much larger than the triangle. This indicates a large uncertainty in the calculated volume fractions. It is clearly seen that for the salt and HA series, when the concentration of the 3rd components increases, the volume fraction of the 3rd component also increases.

Table 14 shows the resulting calculated volume fractions for all series. The volume fractions for the protein series were negative.

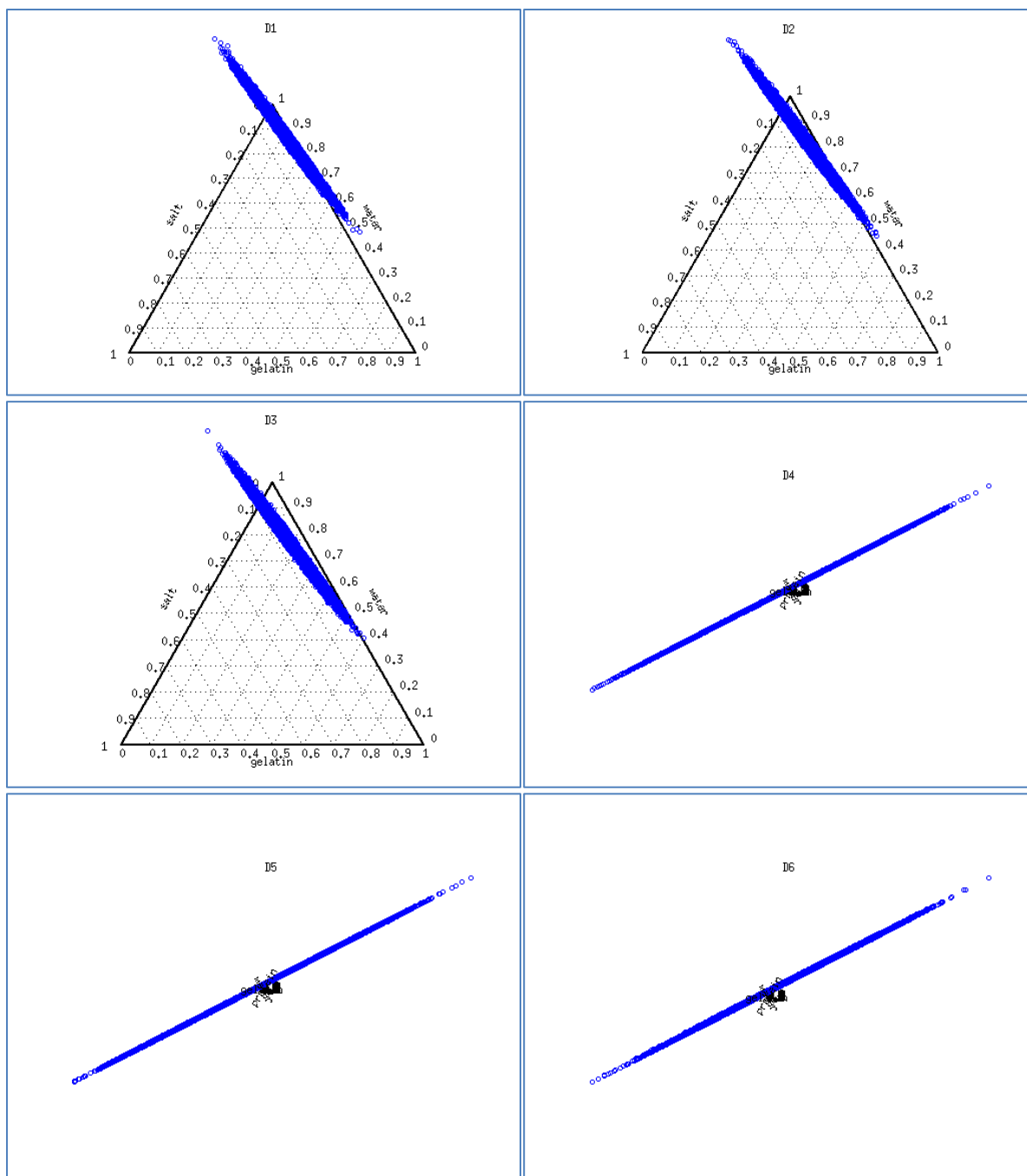


Figure 28 : Ternary plots of volume fractions of samples decomposed to salt, water, gelatin (test tube D1, D2, D3) and protein, water, gelatin (test tube D4, D5, D6)

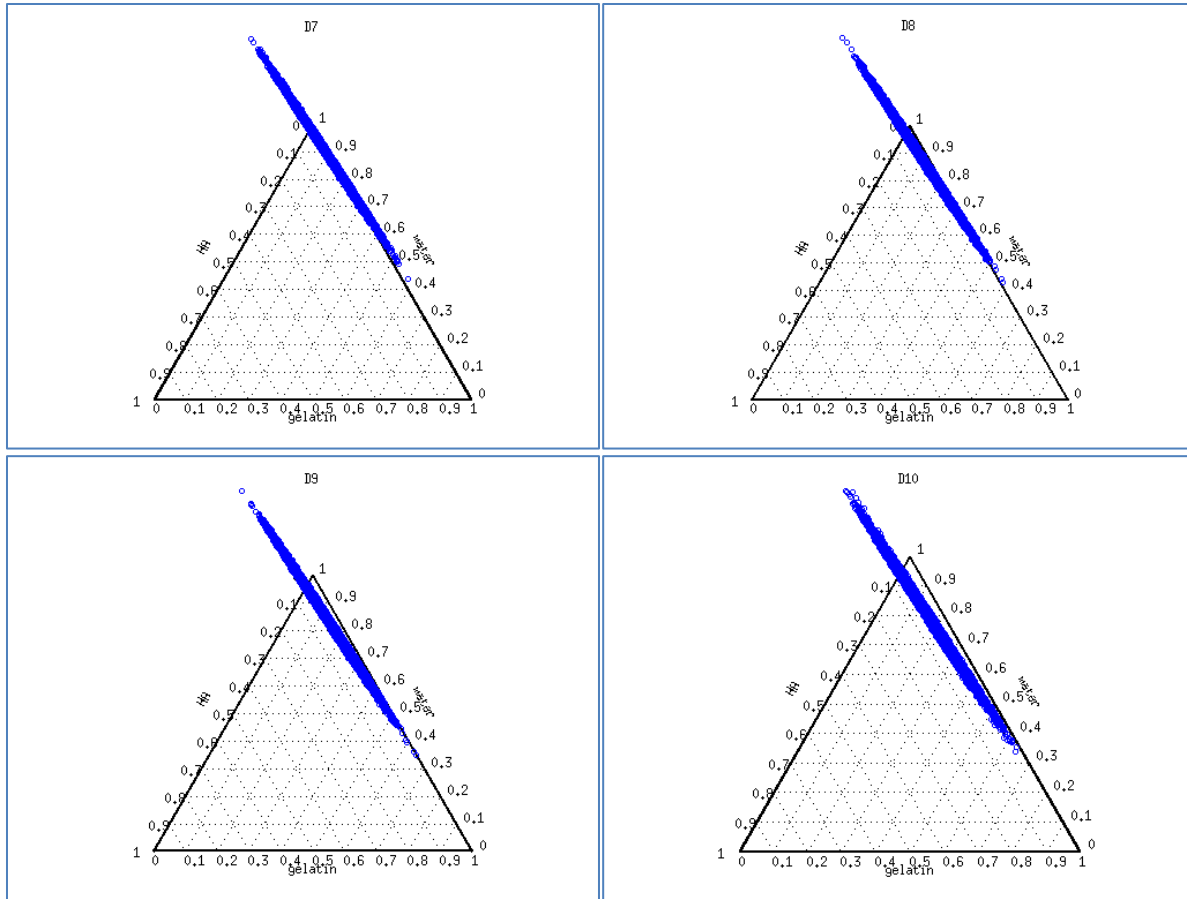


Figure 29 : Ternary plots of volume fractions of samples decomposed to HA, water, gelatin (test tube D7, D8, D9, D10)

Table 14 : H3 volume fractions of water, gelatin and 3rd component

Samples		H3 (v_i)		
Salt Series	v of water	v of gelatin	v of salt	
D1	0.869	0.114	0.018	
D2	0.829	0.137	0.034	
D3	0.777	0.165	0.057	
Protein Series	v of water	v of gelatin	v of protein	
D4	-0.402	-1.401	2.803	
D5	0.676	-0.323	0.647	
D6	4.621	3.663	-7.284	
HA Series	v of water	v of gelatin	v of HA	
D7	0.896	0.094	0.010	
D8	0.868	0.111	0.021	
D9	0.836	0.130	0.034	
D10	0.796	0.158	0.047	

3.3.5 Conclusions

In this study, the three material decomposition method was evaluated for mixtures of demineralized water, gelatin and a 3rd component (salt, protein or hydroxyapatite).

For CT numbers averaged over a volumetric region, maximum relative differences of mass fractions were 8% and 15% for mixtures of salt and HA respectively. The discrepancy was most likely caused by biased CT numbers. The bias was produced by the Siemens image reconstruction algorithm which is not designed for quantitative measurements. The problematic case was a decomposition of the protein mixture: (i) base material triangle was flat since gelatin and protein had approximately same CT numbers, (ii) chemical composition of protein was known with limited accuracy only. As a result, some volume fractions were negative.

For individual voxels, the volume fractions were strongly affected by statistical noise. For instance, more than one quarter of all volume fractions for the salt mixture was negative. The statistical noise cannot be easily eliminated in case of contemporary clinical CT scanners. In fact, the presented measurement was done with the highest possible tube current.

Both CT number diagrams and ternary diagrams were useful for the visualization of data.

4 Future Work

In this thesis, the accuracy of the three material decomposition method was evaluated for mixtures of water, gelatin and a 3rd base material (salt, HA, and protein) scanned with Siemens SOMATOM Definition Flash scanner. Limited knowledge about the chemical compositions of gelatin and protein hampered a fair evaluation of the three material decomposition method. Laboratory experiments should be performed using three base materials of known chemical compositions. Some chemicals can be used such as agar instead of gelatin and bovine serum albumin (BSA) instead of protein powder.

Phantoms with well-known chemical compositions of materials should be used for evaluation of the iterative reconstruction algorithm performance and accuracy of the iterative reconstruction algorithm and related uncertainties.

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Appendix

Histograms of Selected Regions for Study 3

This appendix contains histograms which relate to Study 3. The histograms of all samples (from D1 to D16) that were plotted for both 80 kV and Sn140 kV to show distributions of CT numbers for voxels in selected volume regions. All histograms (except D6 and D10) have Gaussian shapes. Histograms of D6 and D10 samples, which contain highest concentrations of protein and hydroxyapatite, respectively, have outliers. These outliers were caused by air bubbles. To exclude these voxels from the process, the histograms provide a guide for accurate selection.

