Correlation of Pre-Operative Cancer Imaging Techniques with Post-Operative Gross and Microscopic Pathology Images

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Abstract

In this paper, different algorithms for volume reconstruction from tomographic cross-sectional pathology slices are described and tested. A tissue-mimicking phantom made with a mixture of agar and aluminium oxide was sliced at different thickness as per pathological standard guidelines. Phantom model was also virtually sliced and reconstructed in software. Results showed that shape-based spline interpolation method was the most precise, but generated a volume underestimation of 0.5%.

Keywords: Tomographic Image Processing, Volume Reconstruction, Biomedical Image Processing

1 Introduction

Medical imaging techniques have evolved dramatically over the last two decades. The increase in acquisition and processing speeds, resolution and availability has fostered their widespread use as a diagnostic and assessment tool. However, in cancerous tissue, cellular-level features play a fundamental role in determining the stage and type of carcinoma, as well as its local metabolic behaviour. To date, the gold standard for analysing tissue at these high resolutions is by taking a sample (biopsy) and analysing it under a microscope, which is a highly invasive procedure. The current study aims to retrospectively bridge the gap between post-operative pathology and diagnostic imaging, by fusing pathological findings to pre-operative PET-CT scans. Upon alignment of both datasets, clinical oncologists will be able to identify and match certain pathological features in the pre-operative images. This new insight could potentially help them to better predict cancer staging and prognosis from diagnostic images, therefore avoiding unnecessary surgery.

The challenges of this study are the disparity in image resolution between modalities, low sampling rate in the transverse plane and the non-linear deformations undergone by lung tissue during the different clinical stages. To date, simulations with a synthetic tissue-mimicking phantom have been used to test several volume reconstruction algorithms and methods.

2 Materials and Methods

Several synthetic tissue-mimicking phantoms have been used to test the performance of the different algorithms implemented in this project. Its shape was especially designed in CAD software to include several features useful for testing and challenging different volume reconstruction algorithms (see Figure 1). Materials tested include poly(vinyl alcohol) and agar gelatine, the latter showing the most appropriate mechanical properties for our purpose. Aluminium oxide is added as scattering agent to make the material opaque in the x-ray spectrum.

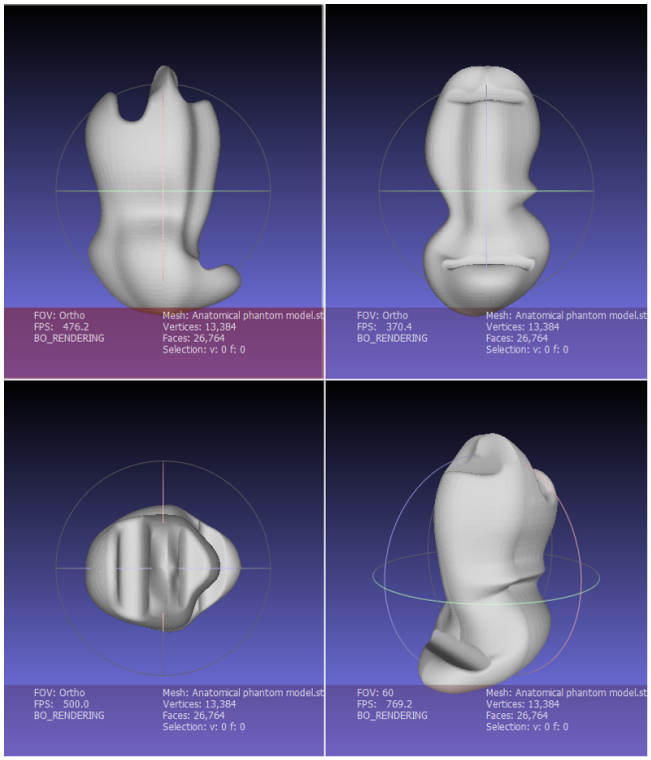

Figure 1: Original phantom design

A custom-designed mould has been 3D-printed to produce the phantom samples. Figure 2 shows a sample cross-section of the phantom in both x-ray and visible spectra.

One of the main challenges of this project is to truthfully reconstruct the original volume and shape of the tumour from tomographic slices. The main reason behind this complexity is because lung carcinomas can adopt highly unpredictable, heterogeneous shapes, which involve fast-changing features along its surface. Combined with the fact that lung tissue has a spongy texture and therefore thin slices cannot be produced without tearing the sample, reconstructing the specimen volume from discrete pathology slices remains an ill-posed problem, as per basic sampling theorem directives. One of the motivations for using a phantom has been precisely the availability of a ground truth model to compare our reconstruction against.

Shape-based interpolation method has been used, first developed by Raya and Udupa [1]. It consists of first segmenting the image to generate a binary mask of the slice, where pixels belonging to the shape of interest are represented by boolean true values. Next, the binary image is converted into a grayscale image, wherein the grey value of a pixel represents the shortest Manhattan distance to the cross-sectional boundary of the binary mask. As a convention, points inside the boundary (i.e. belonging to the shape) are assigned positive distances, and negative values are assigned to outsiders. Those grey values are then interpolated along the z-axis. The non-negative values of the resulting volume constitute the interpolated object.

In our first experiments, several agar phantoms were embedded in a bespoke slicing rig and slices were made at regular intervals (2.5 mm). With the use of a digital camera (Canon EOS M3, Canon Inc., Tokyo, Japan), pictures of each cross-section were taken (see example in Figure 2 right). Next, all photographs were processed to segment the phantom region of interest. Two segmentation approaches were tried: colour thresholding and region growing. The former is based on absolute pixel colour values, whereas the latter depends on the gradient of the scene. In our self-implemented region growing algorithm, the user first needs to interactively select a colour plane, preferably one offering high contrast between the phantom and the surroundings. Three colour spaces are available to choose from, namely RGB, LAB and HSV. Then the user selects a series of seed pixels on the image, which can be any pixel inside the region of interest. If the grey level difference between a

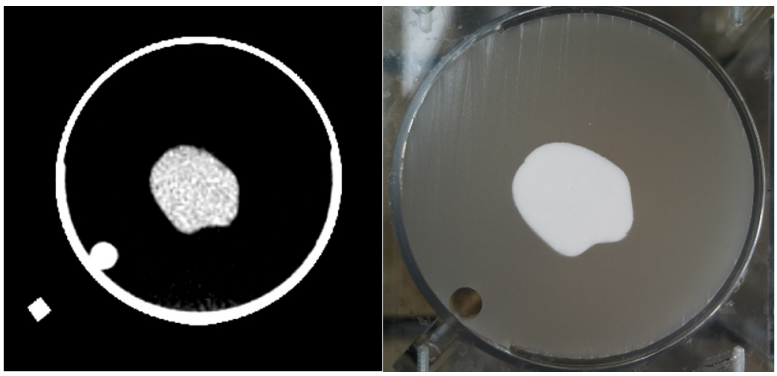

Figure 2: Sample phantom cross-section in x-ray (left) and visible spectra (right)

pixel and a neighbour is less than a given threshold, then the neighbour is included in the region of interest. Otherwise, the neighbour is defined as an outsider. The algorithm iterates until convergence is reached.

3 Results

Initially, several agar phantoms were physically sliced at $2.5mm$ intervals. A picture of a fiducial marker of known size was also taken to establish a relationship between pixel size and real world units. The phantom area was segmented using the algorithms mentioned above. The volume recovered on all experiments laid between 92% and 93% of the ground truth value (measured to be $48,864mm^3$).

At this point the question was whether this underestimation was intrinsic to the interpolation method, or due to imprecisions in the segmentation routine, or a combination of both. Therefore, in order to isolate the interpolation problem, it was proposed to perform a virtual slicing of the original CAD volume and try to reconstruct it from the subset of slices. This way the binary masks were intrinsically defined by the volume cross-sections, avoiding the need to segment the images.

When designing the experiment, however, another question arose: what position should we start slicing our model at? The obvious answer seemed to be at the apex. Whilst this is possible with a virtual model, on an embedded phantom or real carcinoma it is very difficult to perform a cut which corresponds to the plane where the very first distinguishable feature situated on the apex shows. Therefore, this randomness in the position of the first cut had to be accounted for. It was assumed that the first cut could lie in between 0 (i.e. the apex of the object) and one slice thickness, with a uniform probability.

The virtual model was sliced at intervals ranging from 0.5 to $10mm$ in $0.5mm$ steps. For each slice thickness and interpolation method (i.e. nearest neighbour, linear and cubic spline), the routine was run 200 times, introducing a random offset at each iteration. Results are shown in Figure 3. It can be observed that in the region of interest (i.e. slices from $1mm$ up to $5mm$ thickness), nearest neighbour provides the most accurate results, and cubic spline shows a systematic volume underestimation of 0.5%. In order to verify these results, the original phantom CAD model was divided in quarters, and each new shape was reconstructed independently using the same conditions. Results obtained were coherent with those shown in Figure 3.

It was also proposed to perform a local comparison between the ground truth model and reconstructed phantom to evaluate which shape features give the most error. For this purpose, both objects are first converted to point clouds. Then, the reconstructed volume is rigidly registered to the model using Iterative Closest Point (ICP) algorithm. Next, for each point belonging to the generated volume, the distance to its nearest neighbour in the model point cloud is calculated. These distances are then represented in a 3D map, which allows the user to perform a quick qualitative evaluation of the shape reconstructed. After running the routine on the volumes obtained, it was seen that the features giving the largest error were mainly the non-reconstructed shallow valleys and the extrema. These results will be taken into account when designing other phantoms to test our algorithms.

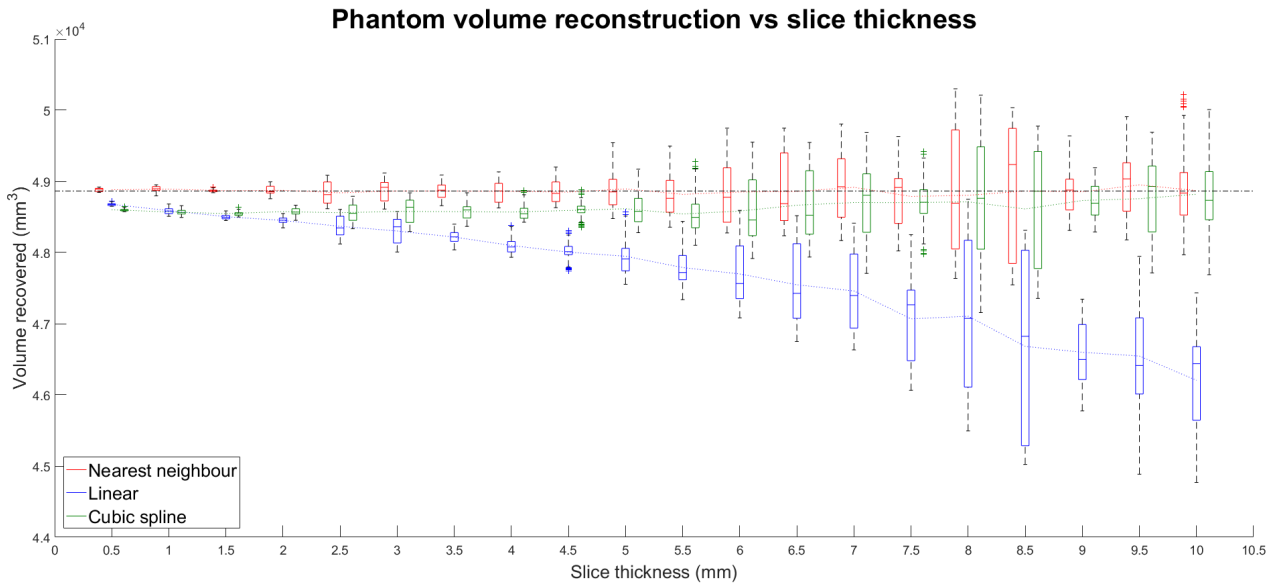

Figure 3: Boxplot showing the volume reconstructed after 200 runs using nearest neighbour (red), linear (blue) and cubic spline (green) interpolation algorithms. Boxes indicate the 25 and 75 percentile of the distribution, horizontal marker indicates the median, and whiskers show the spread of data. Outliers are marked with a cross symbol. Dotted lines represent the evolution of the mean reconstructed value. Ground truth ($48,864 mm^3$) is indicated with a dash-dotted black line.

4 Future work

Future work will be focused on three main areas. **Morphology-based interpolation**: the method proposed in [2, 3] is currently being implemented. It is then going to be tested using the same dataset as used in the shape-based interpolation experiment, so that results can be compared. This method is expected to show better performance around the extrema regions and better handling of topological changes. **Comparison of our algorithms vs commercial software**: the phantom will be scanned in a Computerised Tomography (CT) scanner and its boundary will be delineated by an oncologist on a commercial radiotherapy planning unit. Resulting volume will be compared against ground truth and our implementation. **Trial on human tissue**: volume reconstruction algorithms will be tested on actual lung tissue. Hyperspectral imaging will be tested to explore whether cancerous tissue presents a different absorption spectrum in the near IR region compared to healthy tissue. Automatic tumour segmentation approaches will also be investigated in both gross and pathology specimens.

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