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Research paper

# On the effect of computed tomography resolution to distinguish between abdominal aortic aneurysm wall tissue and calcification: A proof of concept

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ABSTRACT

*Purpose:* The purpose of this study is to determine the optimal target CT spatial resolution for accurately imaging abdominal aortic aneurysm (AAA) wall characteristics, distinguishing between tissue and calcification components, for an accurate assessment of rupture risk.

*Materials and methods:* Ruptured and non-ruptured AAA-wall samples were acquired from eight patients undergoing open surgical aneurysm repair upon institutional review board approval and informed consent was obtained from all patients. Physical measurements of AAA-wall cross-section were made using scanning electron microscopy. Samples were scanned using high resolution micro-CT scanning. A resolution range of 15.5–155 μm was used to quantify the influence of decreasing resolution on wall area measurements, in terms of tissue and calcification. A statistical comparison between the reference resolution (15.5 μm) and multi-detector CT resolution (744 μm) was also made.

*Results:* Electron microscopy examination of ruptured AAAs revealed extremely thin outer tissue structure < 200 μm in radial distribution which is supporting the aneurysm wall along with large areas of adjacent medial calcifications far greater in area than the tissue layer. The spatial resolution of 155 μm is a significant predictor of the reference AAA-wall tissue and calcification area measurements ($r = 0.850$; $p < 0.001$; $r = 0.999$; $p < 0.001$ respectively). The tissue and calcification area at 155 μm is correct within 8.8% ± 1.86 and 26.13% ± 9.40 respectively with sensitivity of 87.17% when compared to the reference.

*Conclusion:* The inclusion of AAA-wall measurements, through the use of high resolution-CT will elucidate the variations in AAA-wall tissue and calcification distributions across the wall which may help to leverage an improved assessment of AAA rupture risk.

## 1. Introduction

Abdominal aortic aneurysm (AAA) rupture represents one of the most fatal surgical emergencies exhibiting a 90% mortality rate [1]. Studies have advocated the potential clinical value of biomechanical indices as a superior measure of AAA rupture risk in comparison to the current standard of maximal AAA diameter alone [2–4]. Doyle et al. have demonstrated that AAA-wall stress analyses can be used to predict localised sites at risk of rupture [5]. Moreover, Xenos et al. have observed that the high wall stresses and corresponding locations of rupture are related to the presence of calcification [6]. Notwithstanding, the precision in measurements of AAA-wall structures in the clinic is a fundamental parameter governing the accuracy of wall stress analyses for the estimation of AAA rupture [2,3].

AAA-wall measurements, indicating structural integrity, are difficult parameters to measure given the spatial resolution of the current clinical imaging modalities [7]. Computed tomography (CT) angiography, using multi-detector CT (MDCT) scanners, is the current standard modality for examining AAA morphological features. Specifically, MDCT is used for both the initial pre-operative rupture risk assessment and the post endovascular aneurysm repair (EVAR) screening [9]. MDCT imaging capabilities and the given spatial resolution (600–820 μm) are limited to measurements greater than 600 μm [10]. This further impedes the accuracy of distinguishing tissue in the presence of adjacent wall calcifications which yield severe blooming artefacts as a consequence of the calcification strongly attenuating x-rays [11]. In this regard, to enable improved prediction of a patient's vulnerability to rupture is an imaging modality capable of evaluating the

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AAA-wall morphological measurements is required.

The evolution of CT angiography technology with novel detectors, reconstruction software and image processing techniques aims to enhance aneurysm diagnostic measurements and support intra-operative endovascular procedures [12]. Specifically, the advent of flat-panel volume CT (FPCT) has been advocated as a potentially superior imaging modality to MDCT providing ultra-high spatial resolution as low as 150 μm [10]. However, the optimal target CT spatial resolution for accurately imaging AAA-wall structural characteristics and distinguishing between tissue and calcification components remains unclear. In this regard, this study characterises the cross-sectional area distributions of both calcified and non-calcified tissue in AAA-walls to determine the optimal target spatial resolution for accurately imaging AAA-wall characteristics.

## 2. Materials and methods

### 2.1. Sample acquisition

Human AAA-wall samples were obtained from eight patients (three ruptured and five non-ruptured) undergoing open surgical aneurysm repair upon institutional review board approval and obtaining informed consent from all patients in a manner that conformed to the declaration of Helsinki and was approved by the hospital's Ethical Research Committee. Segments of AAA-wall were excised from the anterior portion centred on the area of maximum diameter. Table 1 summarises the characteristics of AAA samples. Diameter measurements were made preoperatively using 64-multidetector CT (Siemens sensation 64, Erlangen Germany). Following preoperative CT scan analysis the accuracy of rupture prediction was 100% when correlated with operative findings. The peak voltage was 120kVp and all tomographic slices were obtained with a pixel resolution of 742 μm incorporating a field of view of 380 mm, a slice increment of 0.5 mm and slice thickness of 1 mm and matrix of 512 × 512. Post-operatively, for the purpose of this study, the scans were analysed using Mimics medical imaging processing software (version 17.0, Materialise, Belgium) to identify AAA calcifications ($>$ 1250GV/ $>$ 226 HU) (Table 1). As can been seen in Fig. 1, AAA MDCT scan data examined at 742 μm was very difficult to distinguish between boundaries between intraluminal thrombus (ILT) and wall. The bright white areas at border resemble medial calcifications, as indicated by white arrows, further hampered the identification of the wall's tissue portion due to blooming artefacts.

### 2.2. Structural imaging

To prepare the AAA tissue for *ex vivo* imaging, wall segments underwent a tissue preservation process. The samples were fixed with 100% methanol (Fisher Scientific, product-code:10644795), washed in 100% ethanol (Fisher Scientific, product-code:10020260) and dehydrated in a graded series of increasing ethanol water concentrations (30%–100%). The samples were then dried in a graded series of hexamethyldisilazane (Sigma-Aldrich, product-code:440191) (50% and 100%). This process prevents any deleterious effects to the tissue structure under the intense x-ray voltage source of the scanning electron microscopy (SEM) and micro-CT [13].

### 2.3. Scanning electron microscopy

SEM (Hitachi SU-70 High-Technologies Europe GmbH, Krefield Germany) coupled with an energy dispersive x-ray spectroscope (EDX) (INCA Energy software platform Version4.02 Oxford Instruments, 2006) was utilised to examine wall structures and define the optimal spatial resolution required to differentiate the wall's tissue portion from calcification. For SEM, samples were sputter coated in gold using 35 mA at a deposition rate of 12 nm/min leaving a 24 nm surface coating Emitech K550 (Emitech Ltd., Kent, U.K.). The microscope was operated using an accelerating voltage of 20 keV and a working distance of 15 mm. The presence of calcification was confirmed using EDX by identifying the x-ray signal intensity peaks of Calcium and Phosphorus, the chemical composition of calcification.

### 2.4. Micro-computed tomography

Micro-CT (Xradia versa XRM 500 Carl Zeiss X-ray Microscopy Inc.) scanning was used to examine the contributions of tissue and calcifications in walls at high resolution. The scanning was performed with a 0.4 x optical magnification and 2.5 s x-ray exposure time. The x-ray source was operated at 50 kV and 81 μA and all tomographic slices were obtained with a pixel resolution of 15.5 μm. A low pass filter was used as a balance between the low attenuating tissue and high attenuating calcification. Reconstructions were generated using Xradia XRM reconstructor (version 7.0.2817). The pixel values were rescaled using a standard Hounsfield unit calibration using air, water and hydroxyapatite phantom.

Image slices were examined at 1.55 mm intervals per sample CT scan resulting in a total of 78 image slices analysed in terms of calcification and wall tissue area. The images scanned at 15.5 μm represent the reference spatial resolution as previous studies have reported that at high resolution CT scans at 6.7 μm the calcification can be as small as 15 μm in diameter [14]. This resolution ensures that no calcification is omitted. The image matrix of the reference (15.5 μm) was down-sampled at ten discrete scaling points, to 155 μm which corresponds to the spatial resolution of FPCT. An eleventh resolution point at 744 μm was also analysed which corresponds to MDCT acquired at 742 μm (Fig. 2). All image scaling was performed using ImageJ. Examples of 15.5 μm, 155 μm and 744 μm are illustrated in Fig. 2. A fixed grey value range was defined on the reference image for calcification (100–255GV) and tissue ($<$ 99 GV) on the reference image (15.5 μm) and kept constant for all scaling points to track the difference in area with decreasing resolution. The calcification area fraction (percentage CAF) was calculated as (Calcification area/Total area)*100. Tissue area fraction (percentage TAF) was calculated as (1-percentage CAF). The difference

**Table 1**
Summary of patient details (M = Male F = Female), MDCT corresponding physical wall thickness measurements. (*Blank lines represent the patients with no CT scan available).

| AAA No. | Age | Gender | Rupture | MDCT Measurements | | Physical Measurements | |
|---|---|---|---|---|---|---|---|
| | | | | Diameter (cm) | Global calc volume ($mm^3$) | Avg. wall thickness (mm) | Std dev |
| **1** | 67 | M | Non-rupture | 5.4 | 858.93 | 1.10 | 0.33 |
| **2** | 77 | F | Non-rupture | 5.5 | 4455.77 | 1.46 | 0.46 |
| **3** | 74 | M | Non-rupture | 5.8 | 9156.81 | 1.66 | 0.38 |
| **4** | 77 | M | Non-rupture | 6.5 | – | 1.84 | 0.39 |
| **5** | 77 | M | Non-rupture | 8.9 | 12197.57 | 1.74 | 0.20 |
| **6** | 76 | M | Rupture | 9 | 2569.20 | 1.81 | 0.35 |
| **7** | 71 | F | Rupture | 9 | 5535.68 | 1.50 | 0.23 |
| **8** | 66 | M | Rupture | – | – | 1.64 | 0.25 |