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3D *in vivo* Characterisation of Calcification in Freestyle versus Homograft Aortic Valves

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Introduction

Calcific aortic stenosis is the commonest valve disease in elderly patients in Europe and the United States. Factors implicated in atherosclerosis may contribute to valve calcification and therefore may be amenable to institution of therapeutic measures. In a recent prospective study on a series of asymptomatic patients with severe aortic stenosis, the degree of calcification of the native aortic valve has been shown to be a determinant of prognosis and outcome. In addition, calcification of valve bioprostheses is thought to play a crucial role in their failure. Therefore, availability of a rapid reliable technique for accurately quantifying the degree and pattern of calcification could play a major role in the management of both groups of patients and possibly as a screening tool for “high-risk” individuals. Electron Beam Computed Tomography (EBCT) has been widely used to detect calcium in the coronary arteries and aortic wall. Thus far, routine CT techniques are not able to localise the aortic valve leaflets unless they are heavily calcified because of the movement of the leaflets and aortic ring during different phases of the cardiac cycle. To address this, we have previously described a method utilising contrast enhancement EBT to localise the valve cusps on one occasion which enables repeated scans after that. With the present study we aimed to refine and extend our previous method in order to quantify and localise calcium deposits using a rapid 3-D image registration technique in both native and postoperative bioprosthetic aortic valve leaflets.

Method

A total of 17 postoperative patients (age range 45-75 years) from a prospective randomised trial of Medtronic Freestyle (Medtronic, Inc., Minneapolis, MN) versus homograft root replacement were investigated for EBCT detection and quantification of calcium deposits in the aortic valve leaflets. In this group, 8 received homograft valves (group A) and 9 received a Freestyle bioprosthesis (group B). EBCT scans of the aortic root were performed at 6 monthly intervals after aortic root replacement. For the *in vivo* EBCT, a set of 20-25 transverse tomograms of 3 mm thickness was obtained through the aortic root with the subject breath-holding. Acquisitions were made at 80% of the RR interval. The scan was then repeated during intravenous injection of a contrast medium. Omnipaque 240 (Nycomed Imaging AS, Oslo, Norway) was injected into a vein in the anticubital fossa at a rate of 3 ml/sec, and scans were acquired at 30 seconds after the beginning of the injection.

The examinations based on a sequential back-to-back scan basis. To circumvent the geometrical inconsistencies introduced by the respiratory movements of the base of the heart during the cardiac cycle, we have adapted a rapid multi-resolution 3D image registration scheme. A free-form image registration based on B-spline transformation model was adopted to correct the respiratory induced cardiac deformation. In this study, intensity based cross-correlation coefficient was used as a measure of the degree to which the two images were aligned. The optimal B-spline parameters that maximize this similarity measure were determined using a multi-hierarchical quasi-Newton optimisation strategy.

The quantitative analysis was conducted based on the Agatston scoring scheme. Two independent observers interactively identified the location of the calcified leaflets and defined regions of interest (ROIs) on the enhanced images showing the exact location of the valve leaflets. These ROIs were then automatically overlaid on the corresponding unenhanced ones for calculating the calcium score. For each observer, the process was repeated twice. Both inter and intra-observer variabilities were calculated. In addition, based on the free-form registration results, each aortic valve was normalised as a circular disc whose sectors were labelled as right, left and non-coronary leaflets, respectively.

For each subject, calcified lesions were spatially mapped onto the disc according to their actual locations on the leaflets. The use of this normalisation not only facilitates intra-subject follow-up assessment but also simplifies localisation comparisons. Calcium within aortic sinuses, aortic wall, or both, was carefully excluded from the analysis.

Results

Figure 1 shows an example of colour overlay of the normal and contrast enhanced images before (a) and after (b) registration at three consecutive slice locations. It is evident from the figure that after registration calcium deposits can be clearly identified around the aortic cusps. The quantitative results for these patients are provided in Figure 2. There was a trend for calcification to increase with time in the homografts but not in the Freestyle valves. Of the total 122 volume pairs analysed, the inter-observer variability was 9.2%, and intra-observer variabilities 18% and 13.5%, respectively.

Fig. 1

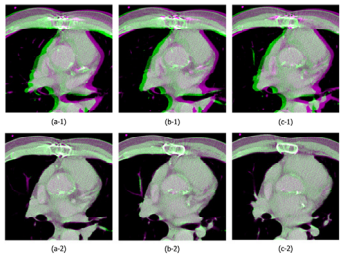
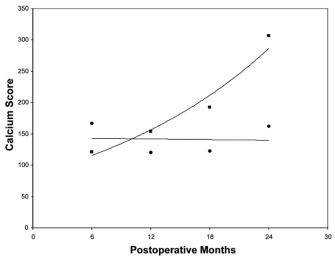


Fig. 2



As shown in 2 samples in Figure 3, calcification was localised mainly at the base of the leaflets in the area of the native aortic annulus which is corresponding to the proximal suture line in the group of patients who underwent aortic root replacement.

In group A, calcification spots have been widely detected in the belly of the leaflets at the latest EBCT scan, affecting the base (Figure 4 top). In group B, minor degrees of calcification remained localised at the suture line and possibly the base of the leaflets and it appeared to be confined into smaller areas of the three cusps (Figure 4 bottom) as compared to the homograft group.

Conclusions

Calcification plays a major role in haemodynamic function and the durability of biological valves after implantation. Accurate localisation of the aortic cusps is therefore essential for quantifying minor degrees of calcification.

This study presents a novel rapid 3D method of serial assessment of the amount and localisation of calcium deposits in bioprosthetic valve transplants. The technique requires one contrast enhanced base-line 3D tomographic data for aligning subsequent EBCT scans that follow the development of calcified regions. The preliminary results demonstrate its potential clinical value for the quantification of the valve calcification.

Fig. 3

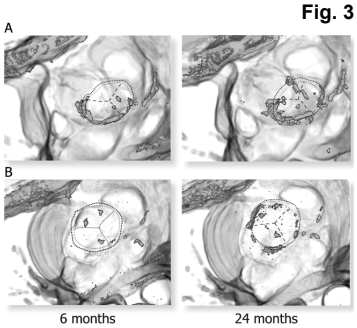


Fig. 4