Automatic detection of inflammatory 'hotspots' in abdominal aortic aneurysms to identify patients at risk of aneurysm expansion and rupture

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INTRODUCTION

Abdominal aortic aneurysms (AAA) are responsible for 1-3% of deaths in men between 65 and 85 years in the western world[1]. Repair of AAA is considered when the aneurysm diameter exceeds 5.5 cm as measured with ultrasound. However, diameter is an imperfect criterion since 60% of AAA >5.5 cm never rupture, while 10-20% of AAA < 5.5 cm do rupture[2,3]. Ruptured AAA cause 80%-90% mortality, so better criteria of AAA expansion and rupture are urgently required. Richards et al[4] in their pilot study, showed that uptake of Ultrasmall Superparamagnetic Particles of Iron Oxide (USPIO) in AAA identifies cellular inflammation and demonstrated that AAA with distinct mural uptake of USPIO (classified as group 3) have a 3-fold increase in aneurysm growth rate compared to AAA with no (group 1) or nonspecific (group 2) USPIO uptake. The classification of "inflammatory hotspots" to stratify patients into the 3 groups was performed manually by trained observers. This manual processing however is time consuming and introduces inter- and intra-observer variability. Due to the manual nature of this classification, the data were analysed on 2D slice-by-slice purely on the basis of presence or absence of hotspot. By automating this assessment, it is possible to assess inflammatory volume throughout the aneurysm which might provide a method to further sub-classify the group 3 patients and further optimise rupture prediction, based on hotspot size and distribution, rather than the manual "presence of hotspot" method alone. Furthermore, this pilot project is now being followed up in the MA3RS study of 350 AAA patients. Manual processing of this large dataset would be impractical so an automated method of AAA classification by hotspot detection is required. We suggest the use of a classification technique (programmed in-house in MATLAB R2013a, Mathworks) which can automatically detect hotspots of inflammation and consequently classify AAA in a robust and efficient way.

MATERIALS AND METHODS

350 patients with asymptomatic AAA >4.0 cm were recruited and imaged using a 3-T MRI Verio (Siemens, Germany) before and 24 to 36 hours after administration of USPIO. T2-weighted imaging was acquired for anatomical data and a multi-echo, gradient-echo T2*W sequence was used to produce T2* maps to detect the accumulation of USPIO within the AAA. Regions or interest (ROI) for the lumen, thrombus and aortic wall were manually defined (SliceOmatic by TomoView) and automatic registration between datasets was applied[5]. The percentage change in T2* value (%ΔT2*) was calculated and displayed as a color scale. The AAAs were then assessed by trained clinicians to detect focal areas ('hotspots') of at least 10 contiguous voxels of USPIO uptake, within the aortic wall and distinct from the periluminal area. At this stage, a threshold of significance for %ΔT2* of 71% was established for the manual classification (based on 95th centile of the %ΔT2* of patients without USPIO). 12 patients classified as group 3 were selected to be processed with our technique for automatic classification. Our method does not use the 71% threshold introduced above, but it rather calculates the %ΔT2* on non-thresholded data to potentially allow better assessment of total distribution of all USPIO within the aneurysm. Due to expected uptake of USPIO in the periluminal area (not corresponding to inflammation, but assumed to be passive transport and 'trapping' of USPIO in periluminal friable tissue[4]) in a significant number of AAA, it was deemed necessary to create a mask in order to exclude the lumen and the periluminal area. These areas had similar ranges of intensity; therefore were segmented together (with k-means clustering, k=4) and were included in a mask. The rest of the processing was applied to both masked and unmasked data, as each method appears to differentiate distributions of USPIO within the various geometries of AAA. In order to detect 'hotspots' of USPIO uptake, an adapted k-means clustering (k=7) algorithm was applied on the %ΔT2* data (masked and unmasked). 2D connectivity was used to identify the 'hotspots' that consisted of at least 10 contiguous voxels and exclusion criteria were applied: the hotspots were rejected if they were in contact with the lumen and accepted only if they were within the aortic wall. The segmented hotspots are automatically saved in individual folders for each slice and the AAA can be automatically classified based on these findings.

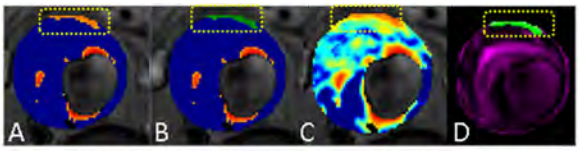

Figure 1: A) %ΔT2* with 71% threshold, B) 'hotspot' detected by clinician, C) %ΔT2* with no threshold , D) 'hotspot' detected by program

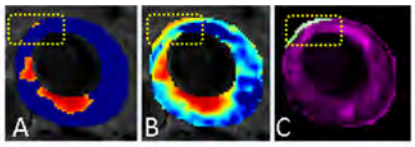

Figure 2: A) %ΔT2* with 71% threshold, B) %ΔT2* with no threshold, C) 'hotspot' detected by program

RESULTS

In the 12 patients from group 3 that were selected to process, the hotspots were identified by our program with a 92% agreement rate in individual hotspots (35 out of 38 hotspots detected) and 100% agreement in classification results (12 out of 12 patients classified as group 3). Importantly, because of the inclusion of non-thresholded data, the automatically detected hotspots appear to be larger (Figure 1). In addition, many extra hotspots were automatically detected and were later accepted as valid after assessment by the trained observers (Figure 2). The total processing time with our program for each patient ranged between 70 to 95 seconds. The corresponding processing time by the observers ranged between 45 to 65 minutes per patient per observer.

DISCUSSION/CONCLUSIONS

The automatic classification program appears to have a very high success rate in fully reproducing the clinicians' manual processing. This software may provide clinicians with more automated, robust and fast data processing and can effectively assist in the decision making process during the assessment of future AAA patients. By using non-thresholded data, extra 'hotspots' of USPIO uptake that were previously ignored by the observers can now be detected. Additionally the 'hotspots' in agreement with the clinicians appear to constitute larger areas. This happens partly due to the fact that the clustering technique adapts to every individual patient, while the 71% threshold used in the manual processing is universal. The processing time of the program is approximately 40 times faster than the manual processing, without taking into consideration the extra time needed for training the observers. The results are fully reproducible such that inter- and intra-observer variability are removed. Additionally, with the use of this tool we have the opportunity to investigate further sub-classification within group 3 of patients.

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