European Journal of Radiology 83 (2014) 1051–1056

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

# Value of volume measurements in evaluating abdominal aortic aneurysms growth rate and need for surgical treatment

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ARTICLE INFO

*Article history:*
Received 14 December 2013
Received in revised form 14 March 2014
Accepted 19 March 2014

*Keywords:*
AAA diameter
AAA volume
Intraluminal thrombus thickness
Intraluminal thrombus volume
Rupture risk
AAA expansion

ABSTRACT

*Purpose:* To examine whether indices other than the traditionally used abdominal aortic aneurysm (AAA) maximum diameter, such as AAA volume, intraluminal thrombus (ILT) thickness and ILT volume, may be superior to evaluate aneurismal enlargement.

*Materials and methods:* Thirty-four small AAAs (initially presenting a maximum diameter <5.5 cm which is the threshold for surgical repair) with an initial and a follow-up CT were examined. Median increase and percentile annual change of these variables was calculated. Correlation between growth rates as determined by the new indices under evaluation and those of maximum diameter were assessed.

AAAs were divided according to outcome (surveillance vs. elective repair after follow-up which is based on the maximum diameter criterion) and according to growth rate (high vs. low) based on four indices. Contingency between groups of high/low growth rate regarding each of the four indices on one hand and those regarding need for surgical repair on the other was assessed.

*Results:* A strong correlation between growth rates of maximum diameter and those of AAA and ILT volumes could be established. Evaluation of contingency between groups of outcome and those of growth rate revealed significant associations only for AAA and ILT volumes. Subsequently AAAs with a rapid volumetric increase over time had a likelihood ratio of 10 to be operated compared to those with a slower enlargement. Regarding increase of maximum diameter, likelihood ratio between AAAs with rapid and those with slow expansion was only 3.

*Conclusion:* Growth rate of aneurysms regarding 3Dimensional indices of AAA and ILT volumes is significantly associated with the need for surgical intervention while the same does not hold for growth rates determined by 2Dimensional indices of maximum diameter and ILT thickness.

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## 1. Introduction

Abdominal aortic aneurysms (AAAs) represent a significant cause of mortality in western societies, becoming more evident with ageing of the population [1]. Rupture is the main complication of aneurysmal disease and despite progress in surgical techniques is still reported to bear a striking mortality of approximately 80% [2,3]. On the other hand, elective repair is currently performed with a perioperative mortality of 3%, thus qualifying aneurysmal disease as one of the more representative pathologies where early detection and intervention reserve such a great gain for patients [4–6].

The need for AAAs surgical repair is determined based on the balance between risk of rupture on one hand and that of surgical intervention on the other. It has long been recognized that rupture risk coincides with aneurysm size, meaning that large AAAs are more rupture prone than small ones [7,8]. Moreover aneurysms tend to increase in size over time with differing growth rates, and if

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http://dx.doi.org/10.1016/j.ejrad.2014.03.018
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left untreated all AAAs would ultimately move towards rupture [9]. Subsequently a means to quantify aneurysm size and growth rate is needed in order to determine appropriate cut-off values for surgical intervention to be recommended. This is traditionally performed using the AAAs maximum diameter criterion. Accordingly large scale randomized clinical trials have set the abovementioned cut-off points which are ≥5.5 cm of maximum diameter and ≥1 cm/year growth rate [4,10,11].

However, the recent advent of 3-dimensional (3D) reconstruction of AAAs from 2-dimensional (2D) computed tomography (CT) images has given access to other variables that quantify their size, raising queries about whether those may be more appropriate to express aneurysm size and growth. Aortic volume is the main index that has been examined in this regard. Subsequently, a Transatlantic debate on the matter was reported with some authors standing for and others against the motion [12–14]. Many authors suggest that maximum diameter represents an adequate measure of AAA size which also predicts adverse cardiovascular outcomes [15]. On the other hand, various study groups indicate that aneurysm volume may be superior in pointing out changes of AAA size and such research has mainly been performed to evaluate changes in AAAs' dimensions after endovascular repair [16–19]. Data as to whether such indices may be useful to evaluate enlargement of small AAAs during follow-up and determine the need for surgical repair are very scarce in the literature [20,21].

In the current study, we examined a cohort of aneurysms, initially being under the threshold for surgical repair and evaluated their growth at a follow-up examination. Some of those aneurysms reached the above-mentioned maximum diameter threshold for intervention to be recommended and consequently underwent elective repair whereas the rest remained under surveillance. We aim to examine if 3D volumetric measurements during assessment of AAA expansion, associate with the need for surgical repair, and compare to the traditionally used maximum diameter measurements.

Moreover taking into account that the great majority of AAAs have a considerable amount of intraluminal thrombus (ILT) which has been suggested to have a critical role in aneurysms natural history and rupture risk, we investigated if changes in ILT related indices such as thrombus maximum thickness and volume may accurately display changes in AAA size over time and associate with the need for repair, as well [22–25].

## 2. Materials and methods

### 2.1. Study population

Thirty-four patients bearing an AAA were included in this single center retrospective study. All aneurysms were initially under the threshold for surgical repair (initial maximum diameter between 4.0 and 5.3 cm) and subsequently underwent a follow-up examination to evaluate aneurysm enlargement. AAAs under examination either underwent surgical repair after the follow-up CT scan due to reaching 5.5 cm of maximum diameter, or remained under observation with serial imaging if they did not reach the above-mentioned thresholds.

### 2.2. Data acquisitions and Image post-processing

All patients had undergone an initial CT scan that either set the diagnosis or was performed during follow-up of a known AAA. Additionally, a follow-up examination at least 6 months apart was obtained. All CTs used in the current analysis were contrast enhanced using intravenous contrast agents. There was a slice thickness of at least 3 mm in order to retrieve required accuracy for diameter, thickness and volume measurements.

From 2D CT images, realistic 3D AAA models were reconstructed using both manual and automatic segmentation for initial and follow up CT scan. For the segmentation process the open source software ITK-SNAP was used [26]. For contrast enhanced aortic lumen a semi-automated algorithm could be used. Initially the user identified AAA lumen entry and exit points while the rest of the procedure was automated and the segmentation was based on identification of intensity regions with an active contour based process. Manual corrections were performed by the user, if needed. For aortic wall however the segmentation was manual due to poor discrimination from surrounding tissues. Briefly, outlines of the outer surface of the AAA and the luminal surface were manually obtained slice by slice and the 3D surfaces were reconstructed from the stack of contours as we have described elsewhere [27]. The whole process lasted about 20 min for each case. For each model four variables were calculated with regard to both initial and follow-up examination: the maximum diameter ($D_{max}$), total AAA volume (AAA_Vol), ILT maximum thickness (ILT_Thick) and ILT volume (ILT_Vol). AAA and ILT volumes were recorded from the inferior border of the more caudal renal artery to the last slice before the aortic bifurcation. This is preferable than only including the aneurysmal sac in order to accurately record changes during follow-up, since for the latter one should use standard anatomic landmarks, such as the renal arteries and the aortic bifurcation. Moreover this is in accordance with the current guidelines and the reported standards for measuring changes in aneurysm size [28]. Additionally, AAA maximum diameter was obtained using orthogonal measurements which according to guidelines and our previously published data, more accurately display aneurysm size than axial measurements [28,29]. All recordings were performed by two independent observers to assess repeatability of measurements.

### 2.3. Study design and statistical analysis

Annual growth rates (GR) with regard to all four indices used to assess aneurysm expansion (GR_Dmax, GR_AAA_Vol, GR_ILT_Thick, GR_ILT_Vol, respectively) were recorded and median values for the whole cohort were calculated. Percentile annual increase was also calculated.

Median values of differences between the two observers obtaining measurements, was assessed for all indices under evaluation. Coefficient of variation was calculated as well as 95% limits of agreement according to Bland and Altman [30].

Furthermore the correlation between growth rates as calculated using the new indices under evaluation and those of the most widely used GR_Dmax was investigated. Spearman's rho determined the correlation coefficient and statistical significance was recorded.

Moreover AAAs consisting our study cohort were divided in two ways:

- According to outcome (surveillance/Group I vs. elective repair/Group II after follow-up) and
- According to growth rate (high vs. low) based on four indices under evaluation (GR_Dmax, GR_AAA_Vol, GR_ILT_Thick and GR_ILT_Vol).

For the latter, aneurysms with GR < median were allocated to the low growth rate group (LGR) whereas those with GR > median to the high growth rate group (HGR).

In order to investigate agreement between outcome and growth rate as it is determined using various indices, contingency between HGR and LGR groups on one hand and Groups I and II on the other, was evaluated. Pearson's $\chi^2$ test was used for this

**Table 1**
Median values and interquartile range (IQR) of growth rate based on measurements of maximum diameter (GR_Dmax), AAA volume (GR_AAA_Vol), ILT thickness (GR_ILT_Vol) and ILT volume (GR_ILT_Vol) are presented. Moreover percentile annual increase of these parameters (median and interquartile range are presented).

| Index | Median (IQR) growth rate | (%) Annual increase (IQR) |
|---|---|---|
| $D_{max}$ | 3.1 mm/year (1.9) | 7.0% (5%) |
| AAA_Vol | 17 ml/year (21) | 15.5% (15%) |
| ILT_Thick | 2.2 mm/year (3.7) | 18% (37%) |
| ILT_Vol | 10 ml/year (21) | 28.5% (37%) |

purpose. Moreover likelihood ratios and sensitivity/specificity of each variable to predict need for repair were calculated.

## 3. Results

### 3.1. Characteristics of the whole study group

For this study, ethics approval was obtained by the institutional review board and all subjects provided informed consent. The median follow-up period between initial and final CT examination was 12 months (range: 6–36). After follow-up there were 19 AAAs that did not reach appropriate thresholds for surgical repair to be recommended and subsequently continued their surveillance program (Group I). Accordingly there were 15 AAAs that required elective repair (Group II). Regarding the whole study group median and interquartile range (IQR) of the growth rates and percentile annual change as determined using the four indices under evaluation are presented in Table 1.

### 3.2. Agreement between observers and measurements

The agreement of measurements between observers is presented in Table 2. Our results are similar to those of others also evaluating AAA diameter and volume change over time [20,21]. Moreover regarding volume increase we found that 25/34 AAAs presented growth rates above the respective upper 95% level of agreement. On the other hand the same applied to 19/34 AAAs with respect to diameter measurements. This means that 6/34 (18%) of AAAs, according to volume measurements presented a growth beyond inter-observer variability while they did not display significant change regarding diameter measurements.

### 3.3. Correlation of the traditionally used $D_{max}$ growth rate to those of AAA volume, ILT thickness and ILT volume

There was a strong correlation between GR_AAA_Vol and GR_Dmax which was statistically significant (Spearman's rho 0.6, $P = 0.002$). Similarly correlation between GR_ILT_Vol and GR_Dmax was strong and statistically significant (Spearman's rho 0.6, $P = 0.001$). Finally only a moderate correlation could be established between GR_ILT_Thick and GR_Dmax (Spearman's rho 0.4, $P = 0.04$). These results are summarized in Fig. 1A–C.

**Table 2**
Agreement between 2 observers outlining AAAs with regard to all four indices under evaluation. 18% of AAAs presented a growth beyond inter-observer variability according to volume but not according to diameter measurements. CV: co-efficient of variation, CI: confidence interval.

| | Mean difference | 95% CI | CV |
|---|---|---|---|
| GR_Dmax (mm/year) | −0.8 | (−4.7, 3.1) | 3.9 |
| GR_AAA_Vol (ml/year) | −1.3 | (−9.3, 6.7) | 8 |
| GR_ILT_Thick (mm/year) | −0.5 | (−3.8, 2.8) | 3.4 |
| GR_ILT_Vol3 (ml/year) | −1 | (−9.6, 7.6) | 8.6 |

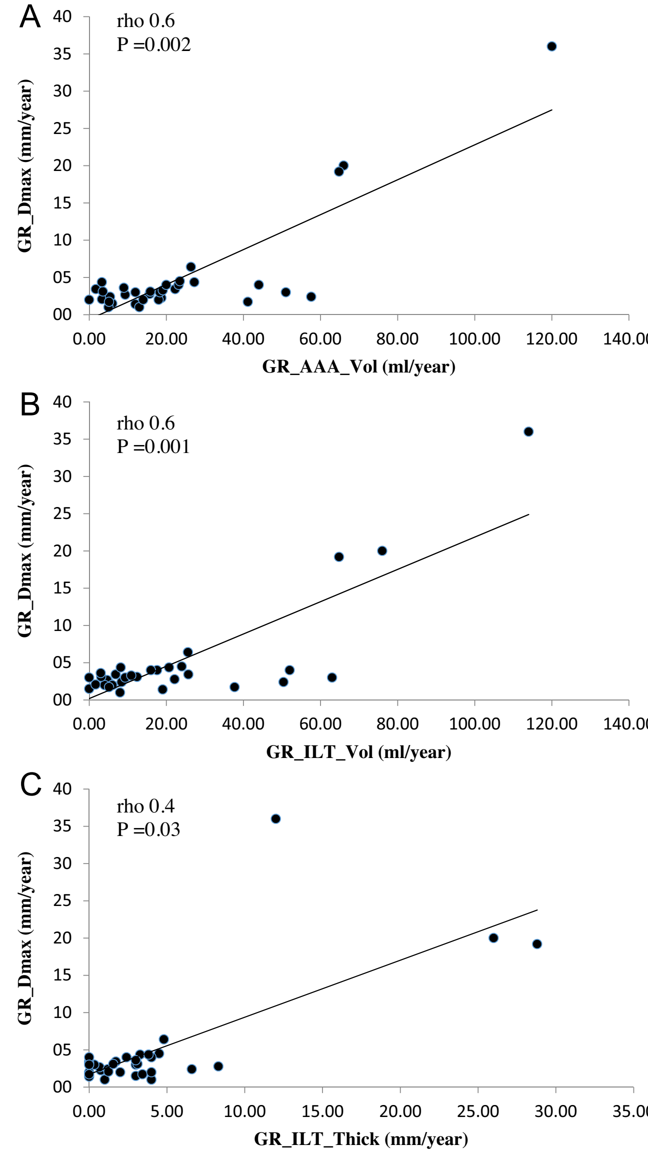


**Fig. 1.** There were strong correlations between growth rates of maximum diameter on one hand and those of AAA and ILT volumes on the other which were statistical significant (A and B). The correlation for ILT thickness was moderate and of borderline statistical significance (C). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

### 3.4. Contingency between groups of high/low growth rate and those of surveillance/surgery: Sensitivity and specificity of measurements to predict need for intervention

Considering that surveillance (Group I) should ideally coincide with slow enlargement (LGR), while need for intervention (Group II) should coincide with rapid expansion (HGR), contingency between HGR and LGR using each one of the indices on one hand and groups I and II on the other was assessed using the Pearson's $\chi^2$ test. These results are summarized in Table 3. With regard to GR_Dmax 10 of the 15 AAAs that underwent intervention were in the HGR and 5 in the LGR group ($P = 0.17$). Taking into account GR_AAA_Vol 12 of the 15 AAAs having undergone surgical correction were in the HGR and only 3 in the LGR group ($P = 0.005$). Regarding GR_ILT_Thick 10 AAAs in the HGR and 5 in the LGR were operated ($P = 0.17$) whereas for GR_ILT_Vol the corresponding values were 12 AAAs in the HGR and 3 in the LGR ($P = 0.005$). Significant

**Table 3**

2 × 2 contingency tables for high and low growth rates as determined using maximum diameter ($D_{max}$), AAA volume (AAA_Vol), ILT thickness (ILT_Thick) and ILT volume (ILT_Vol) on one hand and the outcome (surveillance vs. need for surgical repair) on the other. There were 19 AAAs that were observed while other 15 underwent surgery. Moreover for each variable there were 17 cases of low and 17 of high growth rate. Statistically significant association between groups of growth rate and outcome could be established only for AAA and ILT volumes (*P*-values are reported). With regard to need for surgical repair, likelihood ratios between AAAs in the high and low growth rate groups for all indices under evaluation were calculated as well as sensitivity/specificity of median growth rates.

| | | Surveillance ($n$ = 19) | Surgery ($n$ = 15) | |
|---|---|---|---|---|
| $D_{max}$ ($P$ = 0.17) | Low GR ($n$ = 17)<br>High GR ($n$ = 17) | 12<br>7 | 5<br>10 | Likelihood ratio = 3<br>Sensitivity = 66%<br>Specificity = 63% |
| AAA_Vol ($P$ = 0.005) | Low GR ($n$ = 17)<br>High GR ($n$ = 17) | 14<br>5 | 3<br>12 | Likelihood ratio = 10<br>Sensitivity = 80%<br>Specificity = 74% |
| ILT_Thick ($P$ = 0.17) | Low GR ($n$ = 17)<br>High GR ($n$ = 17) | 12<br>7 | 5<br>10 | Likelihood ratio = 3<br>Sensitivity = 66%<br>Specificity = 63% |
| ILT_Vol ($P$ = 0.005) | Low GR ($n$ = 17)<br>High GR ($n$ = 17) | 14<br>5 | 3<br>12 | Likelihood ratio = 10<br>Sensitivity = 80%<br>Specificity = 74% |

association with need for surgical repair could only be established for AAA and ILT volumes but not for maximum diameter and ILT thickness. With regard to outcome, likelihood ratios between HGR and LGR groups were 10 for 3D indices of AAA and ILT volumes and only 3 for 2D variables of $D_{max}$ and ILT thickness. Subsequently, an AAA that was assigned to the HGR group according to aneurysmal and ILT volume increase, presented a 10-fold risk to having reached appropriate thresholds for surgical repair compared to an AAA in the LGR group. The risk was only 3-fold when HGR and LGR were determined using $D_{max}$ and ILT_Thick. With regard to the observed median growth rates, sensitivity and specificity of each variable to predict need for surgical intervention was calculated. For both 2D indices of maximum diameter and ILT thickness Sensitivity was 66% and Specificity 63%. Superior results were obtained for 3D indices of AAA and ILT volumes with a sensitivity of 80% and a specificity of 74%.

## 4. Discussion

Aneurysmal size as determined by maximum diameter is considered the most significant predictor of rupture with a threshold of 5.5 cm having been identified as the critical value where rupture risk outweighs procedural risks [10]. Although there is wide acceptance and much evidence to support the use of maximum diameter in evaluating aneurysms risk profile, this was mainly established when ultrasound and later CT scan without the advent of 3D reconstruction were used for the diagnosis and surveillance of AAAs [4,11]. Nevertheless, recent advances in imaging allow for the accurate recording of other indices to express AAA size and expansion which may be superior to the traditionally used maximum diameter.

Previous studies have evaluated the possible value of AAA volume measurements for the determination of changes in aneurysm size [16–21]. Prinssen et al. examined volume and diameter changes in aneurysms having undergone endovascular repair and suggested that those regarding sac volume appear to provide earlier reassurance and reduce unnecessary interventions compared to maximum diameter measurements alone [19]. Additionally, Kritpracha et al. indicated that diameter measurements were not sensitive in detecting enlarging AAAs after endografting while volume measurements may be the preferred method for early diagnosis of sac enlargement. Specifically in 27% of their studies with stable maximum diameter, significant AAA volume increase was observed [17]. Similarly, other research groups postulated that using maximum diameter a decrease in aneurysm size can be missed in 14% and an increase in 19% of cases, thus suggesting that volumetry detects sac size changes that are not reflected in diameter measurements [16,18]. These studies examined the role of volume measurements in AAAs after endovascular repair indicating its superiority compared to maximum diameter. To our knowledge there are only scarce data in the literature to address value of volume measurements in evaluating small AAAs enlargement. Recently, Parr et al. highlighted the importance of volumetric measurements in patients undergoing surveillance for AAAs. In their series almost half of the patients with volumetric growth did not have corresponding diameter increases above their respective limit of agreement [20]. Others, studying a group of 28 AAAs recorded a volume growth of 17.3% during a median follow up of 14 months which was significantly higher than $D_{max}$ progression of 8.0% between baseline and follow-up examinations ($P$ < 0.0001) [21]. This may be expected since diameter and volume are related through a power law but in the same time may indicate that since diameter measurements only reflect a single aneurysm dimension in one single cross-section, while volume measurements also take into account the gradual changes of aneurysm morphology, these may detect changes in aneurysm size earlier [31]. Furthermore our results, in accordance to others indicate that overall volumetric measurements have a higher sensitivity for aneurysm growth. In our study cohort a 74% of patients had a volumetric increase above the respective upper 95% level of agreement while the corresponding proportion for diameter measurements was only 56%.

Additionally, it should be mentioned that there were strong correlations which were statistical significant between GR_Dmax on one hand and GR_AAA_Vol as well as GR_ILT_Vol on the other which implies that AAA and ILT volume change over time may be used to evaluate aneurysms' enlargement. Nevertheless and although correlation between volume and maximum diameter increase is expected since the former is a function of the latter, the correlation observed is strong (Spearman's rho 0.6) but still far away from 1 or even 0.8 which would indicate a very strong correlation. Subsequently while volume and diameter growth rates are related, they are not identical and differences do exist.

In order to identify which of the indices under examination may be more appropriate from a clinical point of view, to express AAAs enlargement, we examined the association of the corresponding growth rates with outcome as it is expressed by the subsequent need for surgical intervention. In this analysis the need for surgical intervention is being utilized as the adverse event to which association of volume and diameter measurements is evaluated. This occurs when appropriate diameter thresholds are reached as proposed by current guidelines. Obviously, a harder endpoint i.e. rupture would be desirable and could provide more robust evidence to support our results or even indicate a relevant threshold that would foretell increased rupture risk and indicate need for repair. However in the modern era of strict surveillance protocols for patients bearing small AAAs, rupture is an uncommon event mainly complicating AAAs diagnosed at that time and not those being under observation and having undergone serial imaging. Subsequently, a study that would include a series of AAAs being under surveillance that finally ruptured, to assess their volumetric expansion would be interesting but very unlikely to take place. Alternatively we use an indirect measure to assess aneurysms rupture risk which is the currently used maximum diameter criterion which indicates the need for repair, in order to design the current analyses in a way that meaningful conclusions could be drawn.

Regarding our study methodology, one could argue that a volumetric method used to quantify AAA expansion could not be compared to another using diameter measurements if the maximum diameter is also the variable that defines outcome. Nevertheless this is not the case here since comparisons are being made between growth rates of volumes and diameters while the need for intervention is based on the static value of maximum diameter at one time point (the follow-up CT scan) which is a completely distinct parameter. In other words aneurysm size as expressed by the maximum diameter is used to determine need for repair while comparisons regard increase of diameter and volume over time (growth rates) and their association with the former. To make this more comprehensive we report an example of 2 AAAs from our study cohort. AAA#1 presented a diameter increase from 45 mm to 52 mm (GR_Dmax:7 mm/year) in 12-months' time and remained under surveillance. AAA#2 presented a lower diameter increase from 51 mm to 55 mm during the same time interval (GR_Dmax:4 mm/year) and underwent elective repair. Nevertheless AAA_Vol_GR of AAA#2 exceeded that of AAA#1 (27 ml/year vs. 12 ml/year) which is in accordance with what is suggested by the current analysis.

For this purpose we evaluated contingency between groups of low and high growth rate on one hand and those of outcome on the other. These groups were used to create a $2 \times 2$ contingency table for each one of the examined variables compared with outcome. $P$-values obtained indicate that the results are likely if the null hypothesis of no association between the rows (high and low growth rate) and columns (surveillance and surgery) of the contingency table is true for $D_{max}$ ($P = 0.17$) and ILT_Thick ($P = 0.17$). On the other hand the null hypothesis of no association could be rejected and therefore a statistically significant association between growth rates and outcome could be established for AAA_Vol ($P = 0.005$) and ILT_Vol ($P = 0.005$). More importantly with regard to AAA and ILT volumes a 10-fold risk of AAAs in the HGR group to require surgical intervention was found. The corresponding risk of AAAs in the HGR group when growth rate was determined using $D_{max}$ and ILT thickness was only 3-fold. Therefore AAAs with a rapid volumetric increase were more likely to exceed appropriate threshold of 5.5 cm and be considered suitable for surgical intervention compared to AAAs with rapid increase of $D_{max}$. A representative case of an AAA which presented discrepancies between growth rates of maximum diameter and aneurysmal volume is presented in Fig. 2.

Finally it should be noted that several authors have postulated a critical role of ILT in AAAs natural history and rupture risk. In this regard ILT has been reported to correlate with an increased enzymatic activity as well as decreased arterial wall strength and subsequently an increased risk for rapid AAA growth and rupture [22–24,32]. More importantly an increase in thrombus deposition over time has been suggested to foretell a high risk profile [25]. Therefore it could be suggested that ILT volume besides being critical in terms of AAA mechanisms of progression and rupture also provides an accurate measure of aneurysm expansion over time.

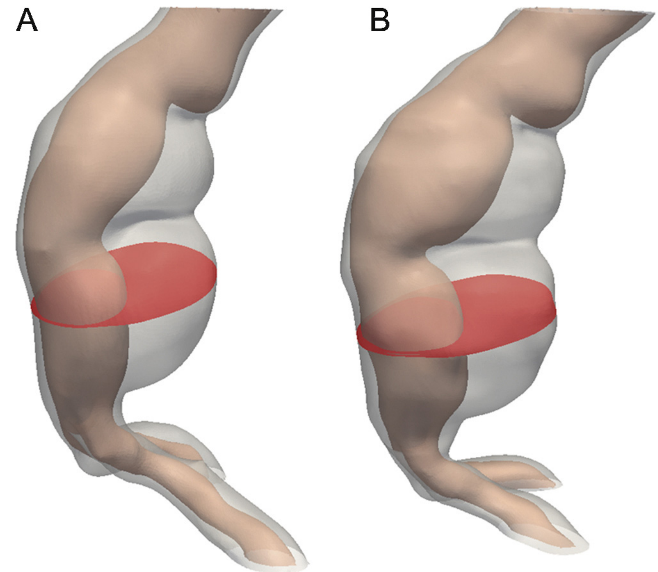


**Fig. 2.** A representative case of an AAA that underwent surgical repair after follow-up, which presented low growth rate (<median) according to the maximum diameter but high growth rate (>median) according to the AAA volume. (A) Displays initial, while (B) presents follow-up examination. This aneurysm presented an initial maximum diameter of 52 mm which after 14 months became 55 mm making it amenable to surgical repair. Growth rate according to maximum diameter was 2.6 mm/year. Aneurysm volume on the other hand presented a growth rate of 42 ml/year (>median). Opaque gray color represents aneurysmal wall, opaque orange color represents aortic lumen, cross-section with red color represents maximum AAA cross-section for initial and follow-up AAA models.

## 5. Conclusion

Three-dimensional indices of AAA and ILT volumes are superior to 2D indices of maximum diameter and ILT thickness regarding their association with outcome in terms of reaching appropriate thresholds to require surgical repair. Therefore from a clinical point of view these may represent more appropriate means to express aneurysm enlargement over time.

## Conflicts of interest

The authors would like to state that they have no conflicts of interest.

## Role of the funding source

The research project was partially supported by the Action «Supporting Postdoctoral Researchers» of the Operational Program "Education and Lifelong Learning" (Action's Beneficiary: General Secretariat for Research and Technology), and is co-financed by the European Social Fund (ESF) and the Greek State.

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