

## Advances in determining abdominal aortic aneurysm size and growth

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**Author contributions:** Kontopodis N conceived the subject and wrote the article; Lioudaki S collected data and critically revised paper; Pantidis D collected data and summarized evidence in Tables; Papadopoulos G collected data and designed images; Georgakarakos E and Ioannou CV had the overall responsibility, revised manuscript and gave final approval for submission.

**Conflict-of-interest statement:** Authors declare no conflict of interest for this article.

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Received: June 6, 2015  
Peer-review started: June 7, 2015  
First decision: August 16, 2015  
Revised: September 6, 2015  
Accepted: December 17, 2015  
Article in press: December 18, 2015  
Published online: February 28, 2016

### Abstract

Abdominal aortic aneurysm is a common pathology in the aging population of the developed world which carries a significant mortality in excess of 80% in case of rupture. Aneurysmal disease probably represents the only surgical condition in which size is such a critical determinant of the need for intervention and therefore the ability to accurately and reproducibly record aneurysm size and growth over time is of outmost importance. In the same time that imaging techniques may be limited by intra- and inter-observer variability and there may be inconsistencies due to different modalities [ultrasound, computed tomography (CT)], rapid technologic advancement have taken aortic imaging to the next level. Digital imaging, multi-detector scanners, thin slice CT and most importantly the ability to perform 3-dimensional reconstruction and image post-processing have currently become widely available rendering most of the imaging modalities used in the past out of date. The aim of the current article is to report on various imaging methods and current state of the art techniques used to record aneurysm size and growth. Moreover we aim to emphasize on the future research directions and report on techniques which probably will be widely used and incorporated in clinical practice in the near future.

**Key words:** Abdominal aortic aneurysm; Size; Growth; Maximum diameter; Volume; Ultrasound; Computed tomography

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**Core tip:** Abdominal aortic aneurysms probably represent the only surgical condition in which size is such a critical determinant of the need for intervention. Recent advances in imaging techniques have raised new possibilities in medical imaging regarding aneurysmal disease making size recordings more accurate and

reproducible than ever. This review article summarizes available techniques, reports state of the art imaging modalities and discusses future perspectives regarding aortic aneurysms' imaging and decision making.

Kontopodis N, Lioudaki S, Pantidis D, Papadopoulos G, Georgakarakos E, Ioannou CV. Advances in determining abdominal aortic aneurysm size and growth. *World J Radiol* 2016; 8(2): 148-158 Available from: URL: <http://www.wjgnet.com/1949-8470/full/v8/i2/148.htm> DOI: <http://dx.doi.org/10.4329/wjvr.v8.i2.148>

## INTRODUCTION

Abdominal aortic aneurysm (AAA) is a focal, balloon-like dilation of the aorta exceeding 50% of its normal diameter which is a common health problem in western societies. Aneurysmal disease is growing in prevalence in the elderly population, with approximately 150000 new cases being diagnosed every year<sup>[1,2]</sup>. The most feared complication of this condition is rupture which is often reported as an intra-abdominal catastrophe since it is accompanied by an overall mortality rate in excess of 80% in the same time that it is ranked as the 13<sup>th</sup> most common cause of death in the United States<sup>[3]</sup>.

Diagnostic and therapeutic protocols regarding AAAs, aim to prevent this disastrous scenario and elective AAA repair with either surgical or endovascular means is being employed for this purpose. Nevertheless and despite the technological progress and accumulated experience which have led to significant improvement of surgical outcomes, current repair techniques are not without complications, while most AAA patients are elderly with several co-morbidities<sup>[4,5]</sup>. Accordingly, the randomized control trials comparing surgical and endovascular techniques for AAA repair report a peri-procedural mortality rate of 0.6% to 6.2% for the former and a 0.6%-2.1% for the latter techniques. Therefore clinicians often have to balance between surgical risk on one hand and risk of rupture on the other in order to set the indication for AAA elective repair<sup>[6-9]</sup>.

Currently aneurysm size and growth rate are being used as the only indices to determine the need for intervention vs surveillance of AAAs since there is firm scientific evidence that increased size and rapid growth indicate a high rupture risk<sup>[10,11]</sup>. In fact AAAs represent the only surgical condition in which size is such a critical determinant of the need to intervene. Although, there are certain limitations in the prognostic value of these variables and there is an ongoing search for additional risk markers to be found (*i.e.*, biomechanical parameters, morphometric characteristics, blood biomarkers, *etc.*) current guidelines for AAA management consider aneurysm size, as it is defined by its maximum diameter (Dmax) as well as aneurysm growth rate (GR) as the only variables in which therapeutic decisions are

based<sup>[10-12]</sup>. Therefore cut-off points have been set by the European Society for Vascular Surgery (SVS) and the SVS (Dmax  $\geq$  55 mm, GR  $\geq$  10 mm/year) that are generally thought appropriate for intervention to be recommended<sup>[10,11]</sup>. Unfortunately landmark studies comparing open surgery vs observation alone took place in the early 90 s, thus before the advents of thin-slice computed tomography (CT), digital imaging and the three-dimensional (3D) reconstruction of AAA surface become widely available. Therefore they have used either ultrasonography (US) (UKSAT trial) or axial CT measurements (ADAM trial)<sup>[13,14]</sup>. On the other hand the most recent randomized trials comparing endovascular aneurysm repair (EVAR) with surveillance, have used orthogonal maximum diameter measurements to determine aneurysm size (PIVOTAL, CAESAR)<sup>[15,16]</sup>. Currently, reporting standards for endovascular aneurysm repair from the SVS recommend that AAA size is most accurately measured using orthogonal measurements, perpendicular to the centerline of flow after 3D reconstruction of the 2D CT images<sup>[17]</sup>.

Moreover in contemporary clinical practice, EVAR becomes increasingly popular among physicians, having overcome open surgery and currently 80% of all AAA elective repairs are being performed by endovascular means<sup>[18]</sup>. This is due to its less invasive nature, reduced peri-operative morbidity and mortality, decreased length of hospitalization, need for blood products, intensive care unit stay, *etc*<sup>[6-9]</sup>. Nevertheless this modality is hampered by the continuous need for surveillance at specific time intervals to assess the successful exclusion of the aneurysm sac from systemic circulation and pressurization. Increase in aneurysm size post-procedurally, usually indicates the need for re-interventions to avoid risk of late aneurysm rupture<sup>[10,11]</sup>. Therefore AAA size and expansion rate except being essential variables to set the indication for elective repair, are also important determinants of the successful exclusion of AAAs post-EVAR. Except Dmax, aneurysm volume has been suggested to accurately display changes in aneurysm size after EVAR.

Therefore in the same time that reproducible and accurate methods to record AAA size are needed, there may be inconsistencies due to different imaging modalities (*i.e.*, US, CT) but also different modes of measurements (*i.e.*, axial vs orthogonal CT measurements, Dmax vs Volume measurements, *etc.*). Subsequently the aim of this review is to report on different imaging techniques and assess their comparability and their value to accurately display aneurysm size and growth and assist therapeutic management of these patients.

## ULTRASOUND MEASUREMENTS

Ultrasound was the initial imaging modality used to record aneurysm size, still being the preferred technique for AAAs screening and surveillance<sup>[19]</sup>. It has the advantage of wide availability, low cost, and freedom from radiation exposure while it has been reported to

have a high sensitivity for the detection of AAAs<sup>[20-22]</sup>. On the other hand US imaging is hampered by the fact that ultrasound waves are disrupted by air and therefore it may not be an ideal imaging technique for organs obscured by the bowel while in large patients, imaging may be ambiguous. In the same time there may be a high operator dependency.

According to Jaakkola *et al.*<sup>[23]</sup>, the inter-observer difference in US was < 2 mm in 65% of the anteroposterior and 61% of the transverse measurements and > 5 mm in 11% of the anteroposterior and 14% in the transverse measurements in 102 observer-pairs for all aortas. This difference was significantly larger with reference to AAAs compared to normal aortas. Specifically, for the latter group 78% of differences were < 2 mm and 4% were > 5 mm whereas corresponding values for AAAs were 53% and 16% respectively. Interestingly, in 5% of cases differences exceeded 10 mm. These authors used the term clinically acceptable difference, which was defined as 5 mm and found 84% of measurements to be below this threshold with regard to the anteroposterior AAA diameter.

Singh *et al.*<sup>[24]</sup> subsequently confirmed abovementioned findings, indicating that both the intra- and interobserver variability were less than 4 mm for all sonographers in measurements of maximal infrarenal aortic diameter for both anteroposterior and transverse Dmax recordings. Specifically they found that 96% and 97% of measurements presented a difference < 4 mm and 88% and 93% of these measurements differed < 3 mm. Nevertheless this report is limited by the fact that almost all examinations regarded normal aortas whereas only one AAA was included.

Ellis *et al.*<sup>[25]</sup> investigated repeatability, observer bias and instrument bias of ultrasound and found that the repeatability of maximum aortic diameter measurement by US was better for anteroposterior than transverse diameter, with coefficients of repeatability 3.0-7.5 mm and 10-15 mm respectively. According to their results, at best a single, experienced observer, using the same instrument may provide aortic diameters using US accurate to within 5 mm, but more commonly such aortic diameter is only accurate to within 8 mm.

Hartshorne *et al.*<sup>[26]</sup> in a more recent study reported that the reproducibility coefficients for differences between different operators were 3 mm for inner to inner wall and 4.2 mm for outer to outer wall indicating that in the same time that there was an expected difference in AAA diameter between the two methods of 0.27 mm, inner to inner wall method was measurably more reproducible.

A recent systematic review studying the reproducibility of ultrasound measurement of the abdominal aortic diameter included 9 studies and found that 6/9 reported intraobserver repeatability coefficients for anteroposterior aortic diameter measurements of 1.6-4.4 mm, which were below the 5 mm level generally regarded as acceptable. In the same time, 5/9 studies had interobserver reproducibility below the level of 5

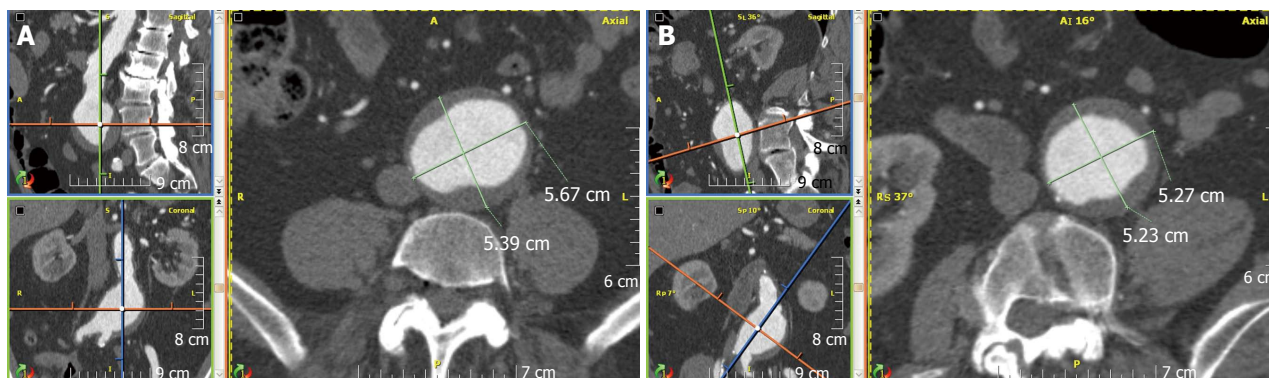
mm but 4/9 reported poor reproducibility ranging from (-2 to 5.2) to (-10.5 to 10.4), which may introduce significant inaccuracies on management of AAA patients. These authors concluded that since various studies use different methodologies with no standardized measurement techniques, a standard training and formal quality assurance of ultrasound measurements are important components of an effective AAA screening program<sup>[27]</sup>.

Overall, among asymptomatic patients, ultrasound detects the presence of an abdominal aortic aneurysm accurately, reproducibly, and at low cost. There is evidence in the literature to support the use of anteroposterior rather than transverse diameter measurement since the latter has worse repeatability<sup>[25]</sup>. Both the external and the internal diameter may be measured bearing in mind that that evidence from the UKSAT study was based on external aortic diameter<sup>[13]</sup>. In the same time the MASS trial, the largest aneurysm screening trial, recorded internal aortic diameter which may be more reproducibly recorded but generally is approximately 3 mm smaller than external diameter, while other screening trials have reported data based on external aortic diameter<sup>[19,28-30]</sup>. Accordingly, ultrasound is the preferred imaging modality for screening, but may be inadequate to accurately record aneurysm size and growth which are important determinants of rupture risk<sup>[11]</sup>.

## 2D Dmax CT MEASUREMENTS

As early as in 1995, Lederle *et al.*<sup>[31]</sup> published a report based on the population of the ADAM trial which included 806 subjects with an AAA indicating that the interobserver difference between local and central CT measurements of AAA diameter was 2 mm or less in 65% of pairs, but in 17% it was at least 5 mm. For intraobserver pairs of central CT re-measurements, 90% differed by 2 mm or less, 70% were within 1 mm, and only one differed by 5 mm, which is suggestive of the superior CT reproducibility and reliability compare to US measurements. Moreover out of 258 ultrasound-measured and central CT pairs, the difference was 2 mm or less in 44% and at least 5 mm in 33%. Finally ultrasound measurements were smaller than central CT measurements by an average of 2.7 mm. These results were produced with the use of older technologies meaning, previous generation CT scanners, use of 10 mm slice thickness without intravenous contrast and measuring maximum external diameter in any direction.

In another report published in 2002 which generally used similar CT parameters as those abovementioned, the authors compared US to CT measurements in aneurysmal aortas and found that the limits of agreement between methods was  $8.7 \pm 7.3$  mm for anteroposterior measurements and  $10.2 \pm 11.0$  mm for transverse measurements. Therefore it could be expected that 95% of differences would be less than 8.0 mm in anteroposterior measurements and less than 10.6 mm



**Figure 1** An abdominal aortic aneurysm after three dimensional reconstruction. In panel A the axis are not perpendicular to the vessel lumen while in panel B they are. An overestimation of the maximum diameter has been observed using axial versus orthogonal measurements.

in transverse measurements. A clinically acceptable difference ( $< 5$  mm) was found in 76% and 67% for anteroposterior and transverse measurements respectively and therefore 1 out of 4 patients scanned, would have a difference greater 5 mm between US and CT measurements<sup>[32]</sup>.

Sprouse *et al.*<sup>[33]</sup> studied a total of 334 AAA patients and found a significantly larger Dmax when this was evaluated with CT than with ultrasound (56.9 mm vs 47.4 mm,  $P < 0.001$ ). Moreover Dmax measured with CT was greater than that measured with US in 95% of cases. The correlation coefficient between these recordings indicated a strong correlation of 0.705, but interestingly, the difference between the two methods was less than 10 mm in only 51%. Limits of agreement exceeded the limits of clinical acceptability and therefore these authors postulated that assessment of AAA diameter with CT and US is not equivalent and that maximal AAA diameter at CT is significantly and consistently larger than maximal diameter at US.

Singh *et al.*<sup>[34]</sup> confirmed these results and indicated that US slightly underestimated the diameter in normal aortas and tended to overestimate the diameter in aneurysmal aortas compared to CT measurements. In 555 US-CT pairs, the absolute differences were  $< 2$  mm in 62%, 60% and 77% in anteroposterior, transverse and maximum diameter in any plane, respectively. The corresponding figures for an absolute difference of 5 mm or more were 14%, 18% and 8%, respectively while variability increased with increasing diameter.

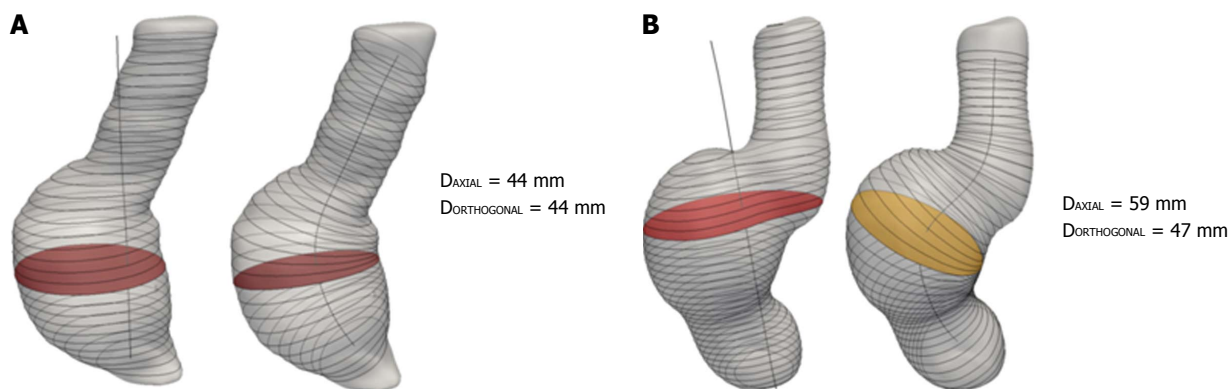
Overall, it may be suggested that CT is more reproducible than ultrasound, in the same time that standard axial CT imaging generally results in larger diameter recordings which likely reflects the fact that aortic cross-section obtained by axial imaging does not account for vessel tortuosity or may be elliptical and therefore could overestimate AAA size. In the same time that the advantages of portability and decreased expense have made ultrasound the preferred diagnostic technique for aneurysm screening and surveillance CT is the primary modality for operative planning, given its capacity to determine the extent and morphology of the aneurysm<sup>[11]</sup>.

### 3D Dmax CT MEASUREMENTS

The advents of thin-slice CT, digital imaging and more importantly technological advances that have made 3D-reconstruction of AAA surface feasible, have recently allowed for more accurate measurements of AAA size parameters. Many vascular centers currently use modern imaging and analytic technology that allows precise computer-based measurement as well as automatic centerline determination. Therefore and in order to avoid overestimation of the AAA maximum diameter on axial CT slices due to vessel tortuosity and elliptical cross-sections, reporting standards of the SVS recommend that diameter should be measured in an orthogonal plane, meaning perpendicular to the vessel centerline of flow<sup>[17]</sup>. Figure 1 presents an AAA after 3D reconstruction, using commercially available software and displaying differences between orthogonal and axial diameter measurements.

Sprouse *et al.*<sup>[35]</sup> compared between US, axial CT and orthogonal CT measurements of AAA maximum diameter as obtained after 3D reconstruction. They suggested that mean axial Dmax was significantly larger than that measured by US or in an orthogonal plane. The difference between US and orthogonal CT measurements was insignificant. Moreover these authors indicated that when aortic angulation was  $< 25^\circ$ , axial CT, US and orthogonal CT Dmax were similar while, when aortic angulation was  $> 25^\circ$ , axial CT Dmax was significantly larger. The limits of agreement between axial CT measurements and those obtained by US or orthogonal CT were poor and exceeded clinical acceptability (5 mm). On the contrary the variation between US and orthogonal CT recordings was minimal with an acceptable limits of agreement.

Similarly, Manning *et al.*<sup>[36]</sup> compared between ultrasound, axial and orthogonal maximum diameter measurements in order to record discrepancies between various methods. They indicated that the mean of each series of readings on CT was significantly larger than the mean US measurement, and that CT measurements also differed significantly from each other. The axial CT diameter was larger than the orthogonal by a mean



**Figure 2** Two abdominal aortic aneurysms are presented after three dimensional reconstruction of the computed tomography images. In the left panels cross sections are perpendicular to the y-axis of the CT scanner coordinator system (axial), while in the right panels cross-section are perpendicular to the centerline of flow (orthogonal). Large discrepancies between methods may be encountered in case of high regional asymmetry as in case B. CT: Computed tomography.

of  $2.4 \pm 5$  mm. The US diameter was smaller than CT axial by  $9.6 \pm 8.0$  mm and CT orthogonal diameter by  $7.3 \pm 7.0$  mm, while AAA size did not significantly affect these differences. Seventy-eight percent of 120 pairs of intraobserver CT measurements and 65% of interobserver CT measurements differed by  $< 2$  mm. Therefore, CT-based measurements of aneurysm size tended to be larger than the US measurement and axial are consistently larger than orthogonal diameters.

Others have compared between US and CT measurements and found a larger AAA maximum diameter of 2.1 mm with the latter modality, in the same time that limits of agreement were -5.5 to 9.6 mm, exceeding clinical acceptability. Mean difference was higher in subjects with a maximum diameter between 50-55 mm as assessed by ultrasound compared to those presenting with larger AAAs above 55 mm (3.9 mm vs 1 mm). Remarkably, 70% of those patients with a US recording between 50 and 55 mm had CT scans revealing diameters greater than 55 mm. Therefore these authors conclude that significant differences between imaging modalities do exist and recommend AAAs measuring  $> 50$  mm on US, to undergo earlier CT imaging<sup>[37]</sup>.

Our study group specifically examined discrepancies between axial and orthogonal CT measurements in sixty CT scans and showed that there is a consistent overestimation of AAAs maximum diameter when measured on an axial plane. Although the mean difference between measurements was low there was a wide range among cases that can change therapeutic decisions in a significant 20% of cases. Asymmetry of the axial sections can easily be determined from 2D CT slices by introducing Shape Index which is defined as: Section minor axis/section major axis. In case of high regional asymmetry (shape index  $\leq 0.8$ ) an overestimation of maximum diameter by  $> 5$  mm might be expected. In this instance orthogonal measurements should be pursued to determine actual aneurysm size. For shape index  $> 0.8$ , axial measurements alone are usually adequate. Figure 2 presents axial and orthogonal dia-

meter measurements for two AAAs, one of which would display large discrepancy due to high regional asymmetry. Moreover we were the first to examine discrepancies in growth rate determination using various CT measurements. There were insignificant differences in growth rates when determined using orthogonal or axial measurements in both examinations (median growth rate: 2.3 and 3.3 mm/year respectively  $P = 0.2$ ) in the same time that there were remarkable differences when orthogonal measurements were used at initial and axial measurements at follow-up examination or vice versa (median growth rate: 4.9 and 0.9 mm/year respectively  $P < 0.001$ ). Therefore growth rates of AAAs should be calculated using the same method of measurements in both CTs otherwise there can be significant discrepancies<sup>[38]</sup>.

Overall it can be concluded that the advents of thin-slice CT, digital imaging and readily available software to perform 3D-reconstruction, have rendered previously described measuring methods out-of-date. However, one should bear in mind that current thresholds to determine the need for intervention are based on older studies, using less sophisticated techniques. Therefore if someone considers the UKSAT trial, surgical repair would be indicated for aneurysms  $> 55$  mm of maximal US anteroposterior diameter<sup>[13]</sup>. According to the study by Manning *et al.*<sup>[36]</sup>, the currently recommended CT measurement technique, shows consistent bias toward a larger diameter value than US measured diameter, with a mean difference of 7 mm which means that, what would be a 56 mm aneurysm by current standards is actually a 49 mm aneurysm using UKSAT method which would lead to the surveillance rather than surgical correction of this aneurysm. The current SVS reporting standards recommend that diameter should be recorded perpendicular to the line of blood flow in order to display actual aneurysm size<sup>[17]</sup>. Nevertheless, diameters measured in this way, actually have not previously been used in the trials that have determined appropriate thresholds for surgical AAA repair. Overall, a summary of studies comparing different techniques to record AAA

**Table 1 Summary of studies comparing between various Dmax measurements**

Ref.	Journal, yr	Variables	Main results	Highlights
Lederle <i>et al</i> <sup>[231]</sup>	<i>J Vasc Surg</i> , 1995	US, CTaxial	US smaller than CTaxial an average of 0.27 cm	Difference < 0.2 cm in 44% and > 0.5 cm in 33% of patients
Jaakkola <i>et al</i> <sup>[23]</sup>	<i>Eur J Vasc Endovasc Surg</i> , 1996	US, CTaxial	Mean AAA anteroposterior CTaxial-US difference was 2.6 ± 3.9 mm. Mean transverse difference was 0.8 ± 4.4	Interobserver differences < 5 mm in 84% of the US and 91% of the CTaxial recordings
Wanhainen <i>et al</i> <sup>[32]</sup>	<i>Eur J Vasc Endovasc Surg</i> , 2002	US, CTaxial	In AAAs the mean diameter did not differ significantly	95% of differences between US and CTaxial are expected to be < 8.0 mm in anteroposterior and < 10.6 mm in transverse measurements
Sprouse <i>et al</i> <sup>[33]</sup>	<i>J Vasc Surg</i> , 2003	US, CTaxial	CTaxial (5.69 ± 0.89 cm) significantly larger than US (4.74 ± 0.91 cm)	Strong correlation between CTmax and US ( $r = 0.705$ ), but difference < 1.0 cm in only 51% of cases
Singh <i>et al</i> <sup>[34]</sup>	<i>Eur J Vasc Endovasc Surg</i> , 2004	US, CTaxial	Total: US smaller by -0.11 mm, aortas < 30 mm: US smaller by -0.64 mm, aortas 30-39 mm: CT smaller by 0.67 mm, aortas > 40 mm: CT smaller 1.09 mm	Differences > 5 mm are expected in 8% of patients. Variability increases with increasing diameter
Sprouse <i>et al</i> <sup>[35]</sup>	<i>Eur J Vasc Endovasc Surg</i> , 2004	US, CTaxial, CTorth	Mean CTaxial (58.0 mm) significantly larger than USmax (53.9 mm) or CTorth (54.7 mm). Insignificant difference between US and Dorth	When aortic angulation was < 25°, Daxial (55.3 mm), US (54.3 mm), and Dorth (54.1 mm) were similar. When aortic angulation was > 25°, Daxial (60.1 mm) was significantly larger than US (53.8 mm) and Dorth (55.0 mm)
Manning <i>et al</i> <sup>[36]</sup>	<i>J Vasc Surg</i> , 2009	US, CTaxial, CTorth	US smaller than CTaxial by 9.6 mm and CTorth by 7.3 mm	Of all CT recordings, diameter perpendicular to the maximal ellipse on axial sections most closely approximates the findings of US and therefore this most closely approximates criteria used in the UKSAT
Foo <i>et al</i> <sup>[37]</sup>	<i>Eur J Vasc Endovasc Surg</i> , 2011	US, CTorth	US underestimated AAA size compared to CTorth by a mean difference of 0.21 (± 0.39) cm	Limits of agreement were -0.55 to 0.96 cm, exceeding clinical acceptability. 70% of patients with US < 5.5 cm presented CTorth > 5.5 cm
Kontopodis <i>et al</i> <sup>[38]</sup>	<i>Eur J Radiol</i> , 2013	CTaxial, CTorth	CTaxial greater than CT orth by 2 mm (range: 0-12.3 mm)	20% of the CTs presented Daxial above and Dorth below 5.5 cm which is threshold for repair. Growth rates should be determined with either axial or orthogonal technique not interchanging between methods

AAA: Abdominal aortic aneurysm; CT: Computed tomography; CTorth: Orthogonal maximum diameter measured from CT images; CTaxial: Axial maximum diameter measured from CT images; US: Ultrasonography.

Dmax are presented in Table 1.

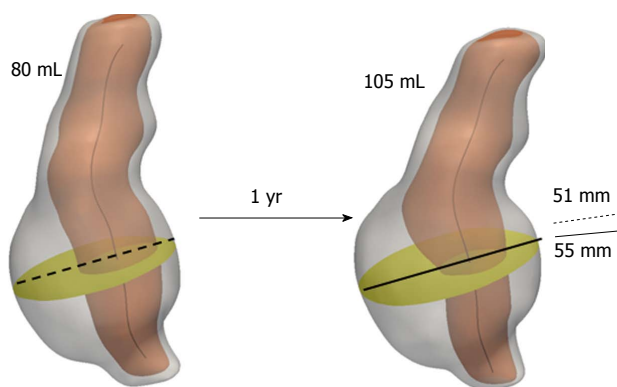
### 3D VOLUMETRIC INDICES

Currently, commercially available software allow image post-processing and accurate as well as rapid volume recording of aneurysmal sac<sup>[39]</sup>. Subsequently this latter variable has been tested against the traditional index of Dmax regarding its accuracy in determining aneurysm size and its sensitivity to capture aneurysm growth over time.

Parr *et al*<sup>[40]</sup> in a study including 57 patients indicated that the reproducibility of measurements regarding both aortic volume and diameter was excellent with an average coefficient of variation < 4%. When they classified size changes according to the 95% limits of agreement for each outcome (aortic expansion: When volume or diameter changes exceeded the appropriate limit of agreement and stasis: When volume or diameter changes were below the appropriate limit of agreement) they found that a significant 42% of patients who had increased aortic volume did not display corresponding axial or orthogonal diameter changes. Therefore despite the fact that total aortic volume and maximum diameter can both be measured reproducibly, volume changes are not always reflected by similar changes in diameter.

Similarly, Kauffmann *et al*<sup>[41]</sup> investigated the ability of a semi-automated segmentation combined with 3D-3D registration between baseline and follow-up examinations to enable fast volumetric follow-up by operators with minimal training in untreated AAA patients to evaluate the software's ability to detect growth. They were able to show an excellent interobserver agreement with a repeatability coefficient < 3 mm for Dmax, < 7% for relative Dmax growth, < 6 mL for volume and < 6% for relative volume growth. Remarkably, using absolute growth, 22/28 patients had volumetric increase above the 95% limits of agreement whereas 18/28 patients had diameter increase above the 95% limits of agreement. Thus, 4/28 (14.3%) of patients had discordance between volumetric and diameter changes during follow-up. These authors conclude that AAA volume was a more sensitive mean to detect AAA growth than Dmax. It should be mentioned that the average time to segment the AAA was < 4 min which shows the ease of this method.

Kritpracha *et al*<sup>[42]</sup> studied 68 patients post-EVAR in order to detect size changes and compared between diameter and volume measurements. They used a cutoff value of 5 mm for diameter and 10% for volume change to define significant size change. The volume recordings identified AAA size change in 81% of studies (15% increase and 66% decrease) whereas orthogonal



**Figure 3** A case of an abdominal aortic aneurysm. An increase of 4 mm/year (may not be considered significant according to current standards taking into account increases > 5 mm), is accompanied by an increase of 20 mL representing 25% of its initial volume which is significant. Volume growth is not always represented in Dmax increase.

Dmax showed AAA size change less frequently (57% of studies, 4% increase and 53% decrease). Volume was stable in 19% of studies, while Dmax showed a greater number of stable AAAs (43%). Among the 20 studies with increased volume, Dmax increased in only 5 (25%).

van Keulen *et al.*<sup>[43]</sup> in a study examining patients having undergone EVAR, indicated that transverse diameter measurements would have missed 63% and orthogonal measurements would have missed 50% of the volume increases, in patients with type II endoleaks. Therefore in the presence of type II endoleaks (in which there is still no consensus about reintervention), volumetry may provide a useful parameter to discriminate between type II endoleaks that either do or do not need reintervention.

In a recent study from our institution we aimed 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. Firstly, we found that 25/34 AAAs presented volumetric growth rates above the respective upper 95% level of agreement while 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. Moreover there was a strong correlation between volume and diameter growth rates which was statistically significant (Spearman's rho 0.6,  $P = 0.002$ ). The most remarkable result of this report is the increased contingency between high growth rate as determined by AAA volume and need for intervention, which was not confirmed for diameter measurements. Specifically, with regard to Dmax growth rates 10 of the 15 AAAs that underwent intervention were in the high growth rate and 5 in the low growth rate group ( $P = 0.17$ ). Taking into account AAA volume 12 of the 15 AAAs having undergone surgical correction were in the high and only 3 in the low growth rate group ( $P =$

0.005). Significant association with need for surgical repair could only be established for AAA volumes but not for maximum diameter. Subsequently, an AAA that presented a rapid volume increase presented a 10-fold risk to reach appropriate thresholds for surgical repair compared to an AAA presenting a slow volume increase. The risk was only 3-fold when accounting for Dmax growth. Sensitivity and specificity to predict need for surgical intervention were superior for volume measurements (Sensitivity 80% vs 66%, Specificity 74% vs 63%)<sup>[44]</sup>. Figure 3 displays an AAA which despite presenting a small Dmax increase, had a rapid volumetric growth.

Overall it can be postulated that according to published literature volumetric indices may be superior compared to Dmax for both untreated AAA surveillance but also to determine size changes post-EVAR<sup>[41,45,46]</sup>. This may be due to the fact that since AAA volumes are much larger than corresponding diameters, absolute changes over time may be bigger and allow for an increased sensitivity in measurements. In a simplified model of AAA expansion a growth of 1 mm in diameter would equal an increase of 10 mL for an AAA of 60 mm length<sup>[40]</sup>. Furthermore, in the same time that diameter measurements only record AAA size at one site, not taking into account changes at other sites, volume measurements also reflect the gradual changes of aneurysm morphology such as lengthening and therefore may be more appropriate in order to record changes in AAA size than maximum diameter<sup>[40,44]</sup>. Findings of studies comparing Dmax vs Volume measurements are presented in Table 2.

## REGIONAL GROWTH MEASUREMENTS

Since aneurysm rupture is in fact a material failure of the aneurysmal tissue to withhold stress due to systemic pressurization which is a localized phenomenon, spatial distribution of mechanical properties of the aneurysmal wall has been suggested to be of critical importance for AAAs natural history<sup>[47]</sup>. Indeed, aneurysm rupture or non-rupture is determined on a pinpoint comparison of wall strength and stress for every point of the aneurysm surface, which would ultimately lead to rupture whenever the forces exerted on the wall, exceed strength of it. Raghavan *et al.*<sup>[48]</sup> explored the regional distribution of wall thickness and failure properties in human AAAs indicating that thickness varied regionally and between different AAAs from as low as 0.23 mm at a rupture site to 4.26 mm at a calcified site. Wall thickness was slightly lower in the posterior and right regions, while the failure tension of specimen strips varied regionally and between AAAs from as low as 5.5 N/cm close to a blister site in the ruptured AAA to 42.3 N/cm at the undilated neck of an unruptured AAA. Similarly, a wide variation of failure stress was recorded ranging from 33.6 to 235.1 N/cm<sup>2</sup> in the same time that there was no perceptible pattern in failure properties along the circumference.

Subsequently the use of universal size variables

**Table 2 Summary of studies comparing between orthogonal diameter computed tomography and volume measurements**

Ref.	Journal, yr	Population	Definition of size-change	Main results
Wever <i>et al</i> <sup>[45]</sup>	<i>Eur J Vasc Endovasc Surg</i> , 2000	Post-EVAR	LOAs	37%, discordance Dmax and volume measurements. A decrease in aneurysm size was missed using Dmax in 14% of cases and an increase in 19% of cases
Prinssen <i>et al</i> <sup>[46]</sup>	<i>Eur J Vasc Endovasc Surg</i> , 2003	Post-EVAR	NA	Volume data resulted in more "good/wait" while Diameter data resulted in more "not good/further diagnostics"-decisions
Kritpracha <i>et al</i> <sup>[42]</sup>	<i>J EVT</i> , 2004	Post-EVAR	10% for volume, 5 mm for diameter	Volume changed in 81% of studies (15% increase and 66% decrease). Dmax changed 57% (4% increase and 53% decrease). Among 20 studies with increased volume, Dmax increased in only 5
van Keulen <i>et al</i> <sup>[43]</sup>	<i>J Endovasc Ther</i> , 2009	Post-EVAR	5% for volume, 5 mm for diameter	Volumetry detected aneurysm growth in 24% and shrinkage in 54% of patients, which was reflected by Dmax in 10.6% and 28% respectively
Parr <i>et al</i> <sup>[40]</sup>	<i>Eur J Radiol</i> , 2011	Small AAAs	LOAs	42% of patients who had increased aortic volume did not display corresponding diameter changes
Kauffmann <i>et al</i> <sup>[41]</sup>	<i>Eur J Radiol</i> , 2012	Small AAAs	LOAs	4/28 (14.3%) patients presented volume increase which was not reflected in Dmax
Kontopodis <i>et al</i> <sup>[44]</sup>	<i>Eur J Radiol</i> , 2014	Small AAAs	LOAs	18% of patients who had increased aortic volume did not display corresponding diameter changes. AAAs presenting rapid volume increase had a 10-fold risk to be operated, while the risk was 3-fold for rapid Dmax increase

LOAs: Limits of agreement; AAA: Ab dominal aortic aneurysm; EVAR: Endovascular aneurysm repair; NA: Not available.

as maximum diameter and volume, in order to record aneurysm expansion is inherently hampered by the lack of information about regional distribution of growth rate. Our study group has previously developed a methodology to record regional growth and applied this to a rapidly growing AAA. For this purpose the centerlines of the aneurysmal wall as well as lumen surfaces were created and used to extract perpendicular cross sections every 1 mm. To determine the aneurysm's pattern of expansion, cross-sectional area change from initial to follow-up examination was plotted against the distance from aortic bifurcation which was considered as the reference point for registration of initial and final CT angiograms. ILT thickness and eccentricity of ILT deposition were also recorded along the aneurysm for both AAA models. Maximum AAA and ILT cross-sectional areas were observed at the same distance from aortic bifurcation that was 4 cm for both AAA models as presented in Figure 4<sup>[49,50]</sup>.

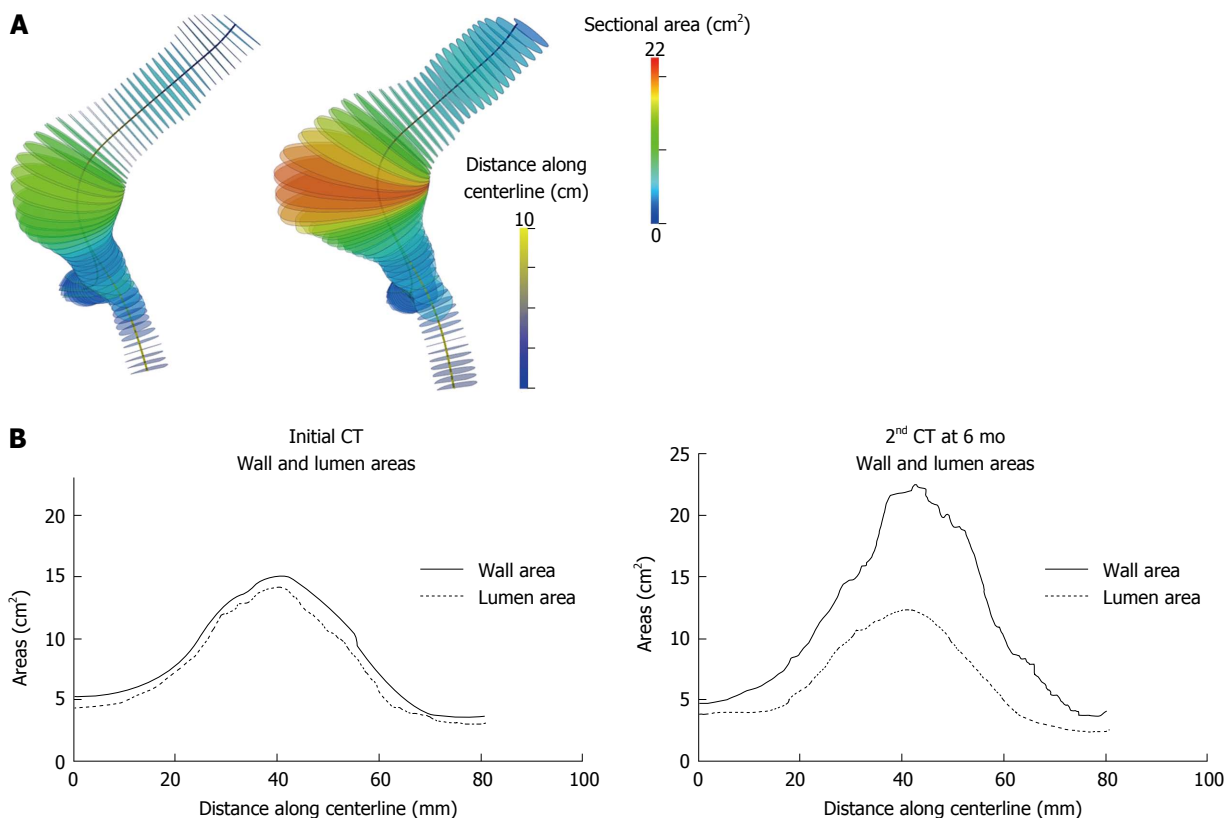
In the same context, Martufi *et al*<sup>[51]</sup> monitored diameter development over the entire aneurysm to record sites of the fastest diameter growth. They suggested that development of an AAA's maximum diameter or its volume over time can assess the mean diameter growth but not the maximum diameter growth. Interestingly, the annual diameter growth measured at the site of maximum expansion was 16%, almost four times larger than the mean diameter expansion of 4.4%. According to this study the site of maximum diameter growth did not coincide with the position of the maximum baseline. Moreover the overall aneurysm sac length increased from 84 to 89 mm during the follow-up, which relates to a median annual longitudinal growth of 3.5% in the same time that the neck length shortened, on average, by 6.2% per year. Therefore these authors postulate that neither maximum

diameter nor volume measurements, are able to record the fastest diameter growth of the aneurysm sac and consequently, expansion-related wall weakening might be inappropriately reflected by this type of surveillance data. In contrast, localized spots of fast diameter growth can be detected through multiple centerline based diameter measurements over the entire aneurysm sac.

## CONCLUSION

Currently, significant technological advancements regarding abdominal imaging have made AAA size and growth recordings more accurate and reproducible than ever. According to evidence reported in the literature which has also been implemented in current guidelines, ultrasound may be used as the primary imaging modality for aneurysm screening and follow up and a policy of ultrasonographic surveillance is advised for small asymptomatic AAAs. In order to accurately capture aneurysm size and determine need but also method (*i.e.*, open surgery or EVAR) for AAA repair, CT imaging is appropriate additional to US, if an AAA is approaching a size requiring intervention, or if rapid growth is suspected. Moreover, standards for reporting on EVAR highlight the significance of orthogonal diameter measurements indicating that preferably, maximum diameter should be measured perpendicular to the centerline of flow with 3D-reconstruction of CT images. The potential role of volumetric indices is also underlined since taking into account that variations in size occur in three dimensions, relatively small diameter shifts that may be difficult to accurately measure with conventional imaging techniques, may be correlated with a significant change in aneurysm volume. Finally regional growth recordings are based in a sound biomechanical ground and therefore may represent the emerging method to





**Figure 4** Cross-sections perpendicular to the centerline with regard to sectional areas for initial and follow-up abdominal aortic aneurysm-models. Maximum sectional areas present values of 22.5 cm<sup>2</sup> and 15 cm<sup>2</sup> respectively. Color scale on the centerlines depicts distance along the centerline with 8 cm representing aortic bifurcation. Sections areas are displayed against distance along the centerline indicating that maximum values are obtained in the same distance from aortic bifurcation (approximately 4 cm). Figure originally published at Kontopodis *et al*<sup>[50]</sup>.

capture aneurysm size and growth which will become increasingly used in the future.

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