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Imaging surveillance after open aortic repair: a feasibility study of three-dimensional growth mapping

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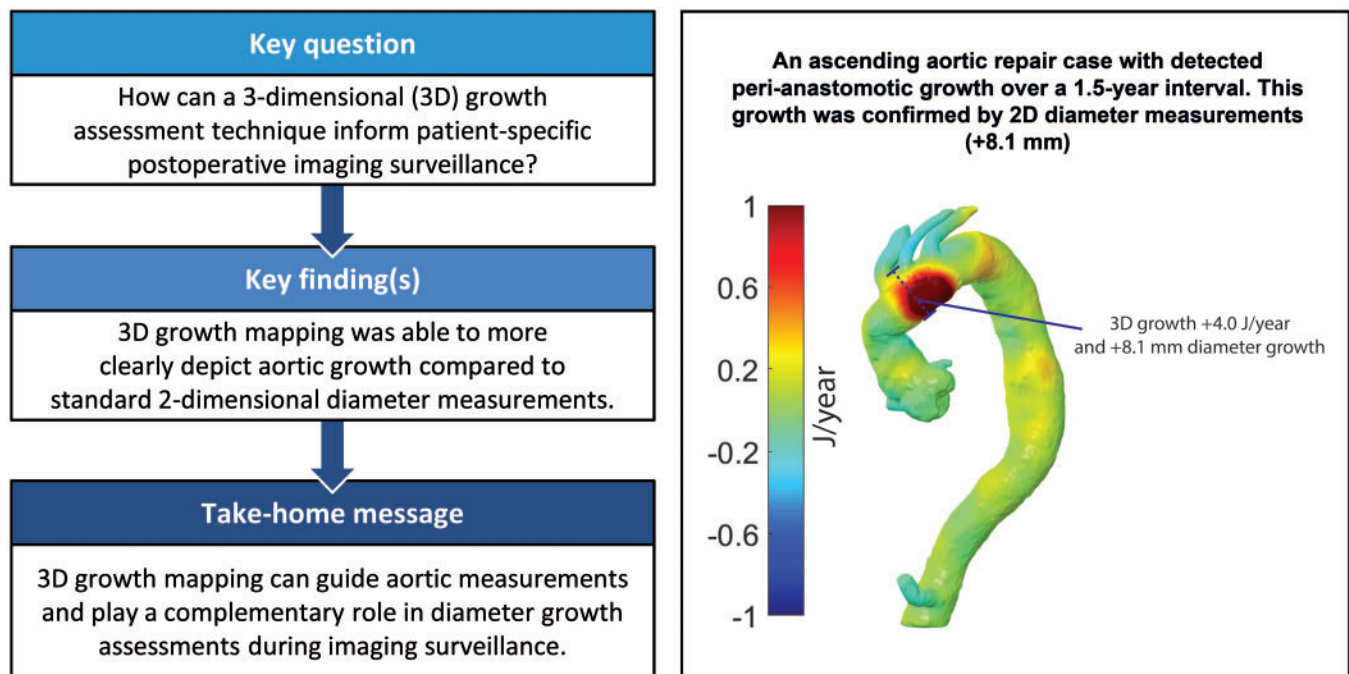
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Abstract

OBJECTIVES: Confident growth assessment during imaging follow-up is often limited by substantial variability of diameter measurements and the fact that growth does not always occur at standard measurement locations. There is a need for imaging-based techniques to more accurately assess growth. In this study, we investigated the feasibility of a three-dimensional aortic growth assessment technique to quantify aortic growth in patients following open aortic repair.

METHODS: Three-dimensional aortic growth was measured using vascular deformation mapping (VDM), a technique which quantifies the localized rate of volumetric growth at the aortic wall, expressed in units of Jacobian (J) per year. We included 16 patients and analysed

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6 aortic segments per patient (96 total segments). Growth was assessed by 3 metrics: clinically reported diameters, Jacobian determinant and targeted diameter re-measurements.

RESULTS: VDM was able to clearly depict the presence or absence of localized aortic growth and allows for an assessment of the distribution of growth and its relation to anatomic landmarks (e.g. anastomoses, branch arteries). Targeted diameter change showed a stronger and significant correlation with J ($r=0.20$, $P=0.047$) compared to clinical diameter change ($r=0.15$, $P=0.141$). Among 20/96 (21%) segments with growth identified by VDM, growth was confirmed by clinical measurements in 7 and targeted re-measurements in 11. Agreement of growth assessments between VDM and diameter measurements was slightly higher for targeted re-measurements ($\kappa=0.38$) compared to clinical measurements ($\kappa=0.25$).

CONCLUSIONS: Aortic growth is often uncertain and underappreciated when assessed via standard diameter measurements. Three-dimensional growth assessment with VDM offers a more comprehensive assessment of growth, allows for targeted diameter measurements and could be an additional tool to determine which post-surgical patients at high and low risk for future complications.

Keywords: Thoracic aortic aneurysm • Imaging surveillance • Aortic growth • Vascular deformation mapping • Open aortic aneurysm repair

ABBREVIATIONS

2D	Two-dimensional
3D	Three-dimensional
CT	Computed tomography
CTA	Computed tomography angiograms
VDM	Vascular deformation mapping

INTRODUCTION

Guidelines recommend imaging surveillance using computed tomography (CT), magnetic resonance imaging, transthoracic echocardiography at 1, 6, 12 months postoperatively, and then annually, to identify post-surgical complications such as progressive growth of the native aorta, dissection or anastomotic complications, although the level of evidence for these recommendations is low (level C) [1, 2]. Failure of the endograft and subsequent reintervention rates are known to be high following endovascular interventions, necessitating strict yearly surveillance. While surgical complications and progressive disease of the native aorta are uncommon, they may take several years following index procedure to manifest, making it difficult to predict which patients are at highest risk of complications and therefore tailor the frequency of follow-up accordingly [3, 4]. Current post-operative imaging surveillance strategies are often inefficient and can lead to excess cost, contrast and radiation. Furthermore, current surveillance strategies vary quite widely between surgeons and institutions and are not based on high-quality evidence [1, 2, 5]. Thus, there is a need for improved imaging techniques to better differentiate patients at high and low risk of complications and progressive growth and guide surveillance strategies.

In addition to questions of the optimal imaging surveillance paradigm, diameter-based imaging surveillance techniques are intrinsically hindered by substantial measurement variability, in the range of ± 2 mm, limiting confident assessment of growth at lower magnitudes [6]. Furthermore, aortic measurements are performed at standard anatomic locations and growth occurring outside of these landmarks can be missed. These measurements are often performed in an axial plane without adequate analysis through multiplanar reconstruction or centreline techniques. In an attempt to address such limitations, a medical image analysis technique for three-dimensional (3D) aortic growth assessment, called vascular deformation mapping (VDM), has been recently

developed [7, 8]. VDM utilizes serial CT angiograms (CTA) to produce a 3D 'heatmap' of thoracic aortic growth that enables the observer to visually appreciate specific regions of aortic growth. Given its use of high-resolution CT data and 3D nature, VDM produces accurate and comprehensive assessments of aortic growth.

The aim of this study was to investigate the feasibility of a 3D aortic growth assessment technique (VDM) to characterize post-surgical growth of the thoracic aorta in patients undergoing imaging surveillance following open aortic repair. Furthermore, we aimed to assess the ability of VDM to guide targeted aortic diameter re-measurements to regions of suspected aortic growth, and to assess the agreement between standard clinical measurements and VDM-targeted growth assessments.

PATIENTS AND METHODS

Ethical statement

This retrospective analysis was performed as part of an Institutional Review Board approved study (HUM00133798), on 18 August 2017 and informed consent was waived.

Study population

We retrospectively identified over 900 patients that underwent open thoracic aortic repair at our institution between 2009 and 2017. A representative sample of 130 patients with various aortic pathologies was evaluated for eligibility (Fig. 1). For this feasibility study, we prospectively defined a required sample size of 16 patients with 96 aortic segments for analysis. Eligibility criteria included (i) 2 postoperative electrocardiogram-gated CTAs, (ii) adequate contrast enhancement and (iii) a CT interval of ≥ 1 year. Patients were excluded if they had either a non-electrocardiogram-gated CT scan, non-contrast CT scan or motion/streak artefacts that would prevent clear delineation of the aortic wall and result in low-quality 3D segmentations. After excluding 114 patients, we included 16 patients for analysis.

Aortic measurements and growth assessment

Based on the standard aortic measurement locations, we analysed 6 unique thoracic aortic segments in each patient as depicted in Fig. 2B [2]. In each patient, we recorded 3 metrics of

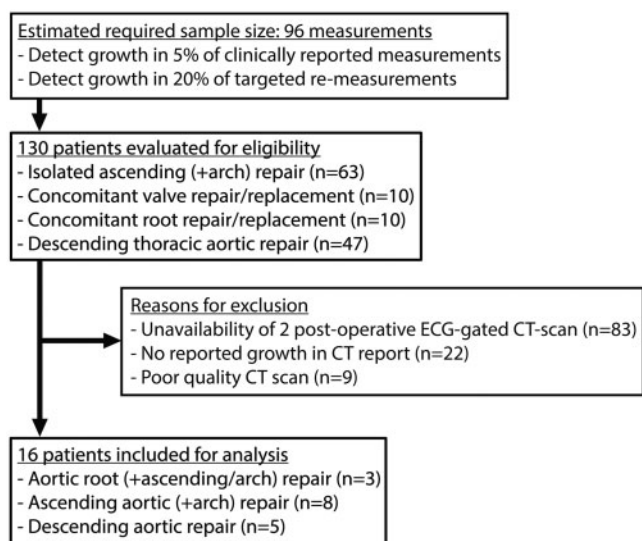


Figure 1: Patient selection flow chart. CT: computed tomography; ECG: electrocardiogram.

growth, including clinically reported CT diameter changes between 2 consecutive CTAs, VDM-derived Jacobian determinant and a targeted CT diameter re-measurement. Clinical diameter measurements were extracted directly from the clinical CTA reports. Aortic CTA measurements at our centre are performed by experienced image-processing technologists in a dedicated 3D laboratory using standard analysis software and centreline-based measurement technique (Vitrea, Vital Images, Toshiba, Tokyo, Japan) and are reviewed by the interpreting Cardiothoracic radiologist prior to publication in the clinical CT report. Targeted diameter re-measurements were performed at all segments using the same 3D analysis software (Vitrea) with the same centreline technique by a researcher with 4 years of aortic analysis experience and were confirmed by a senior researcher with 15 years of cardiovascular imaging experience. Targeted diameter re-measurements were performed at the location of maximal aortic wall deformation based on the VDM analysis, and therefore were not necessarily at the same location as the landmark-based clinical diameter measurements at each aortic segment. 'Growth' was defined as any change >2 mm diameter based on the reported ± 2 mm variability in aortic diameter measurements using centreline technique, and >1.2 (i.e. 20% volumetric expansion) Jacobian volumetric growth (based on measured VDM reproducibility and intrinsic CTA spatial resolution during technical validation) [6, 9, 10]. For the purposes of comparability between cases, all VDM images/figures are displayed as volumetric growth rate (J/year) to normalize for variability in CTA intervals between cases.

Vascular deformation mapping

VDM is a CT-based image analysis technique that allows for accurate and comprehensive measurement of 3D aortic growth between 2 CTAs (Fig. 2A) [8]. Electrocardiogram-gating is required to prevent imaging artefacts. The 1st step consists of a semi-automatic, threshold-based segmentation of the thoracic aorta on CTA images (aortic root to 10 mm below the coeliac artery) using Mimics 22.0 (Materialise NV, Leuven, Belgium) to generate an aortic mask (mask used to delimit aorta during

image registration). This threshold-based approach is reliant on contrast enhancement of the aorta to delineate the aortic wall. Secondly, multiresolution b-spline non-rigid registration is performed to align the thoracic aorta between baseline and follow-up CTAs using open-source registration software (Elastix, Utrecht, Netherlands). Lastly, deformation between 2 postoperative CTA studies is quantified as the determinant of the 3×3 spatial Jacobian matrix, representing the localized (per pixel/voxel) degree of volumetric growth of the aortic wall expressed in units of Jacobian (J). The Jacobian determinant is a unitless value, representing the ratio of localized volume change at a specific point along the aortic wall. The deformation rate is then obtained by normalizing Jacobian determinant with the time interval (J/year). For instance, growth of 0.2 J/year at a specific point on the aortic wall indicates a 20% volumetric growth in that location over the considered time interval.

Statistical analysis

Patient characteristics were expressed as mean \pm SD for continuous variables and categorical variables were presented as frequency and percentage. Our a priori analysis, requiring a sample size of 96 aortic segments, was based on the number segments required to detect growth in 15% more segments with targeted diameter re-measurements compared to clinical diameter measurements assuming Cohen's kappa (κ) of 0.5, $\alpha = 0.05$ and standard error = 0.11 (*kapssi* command in Stata, StataCorp LP, College Station, TX, USA). Pearson's correlation was used to associations between VDM volumetric growth (J) and diameter measurements (both clinical and targeted re-measurements). Agreement of growth assessment (binary yes/no) between clinical measurements and VDM-targeted re-measurements was determined using Cohen's kappa statistic (κ). Statistical analyses were performed using Stata 14.0 (StataCorp LP).

RESULTS

Patient demographics

Patient demographics, clinical risk factors and surgical repair type for the overall cohort and those patients who were included for analysis are depicted in Table 1. Patient characteristics, aortic pathology and surgery type are summarized in the [Supplementary Material](#). In our cohort, ascending aortic replacement was performed in 11 patients, of whom 3 patients underwent concomitant root replacement and 5 patients underwent descending thoracic aortic/thoraco-abdominal repair. No patient had a reported history of connective tissue disease. Details regarding aortic growth are depicted in Table 2. The baseline postoperative CTA was performed 8.3 ± 12.3 months after surgery and interval between baseline and follow-up CTA was 13.3 ± 2.2 months. Follow-up for the entire cohort was 21.6 ± 12.7 months.

Representative cases of aortic growth assessment

Using clinical CTA measurements, we found growth in 9 patients, all of which underwent an ascending aortic replacement. VDM analysis was in agreement in 4 patients (44%). Three-dimensional growth assessment with VDM found growth in 6 patients, which

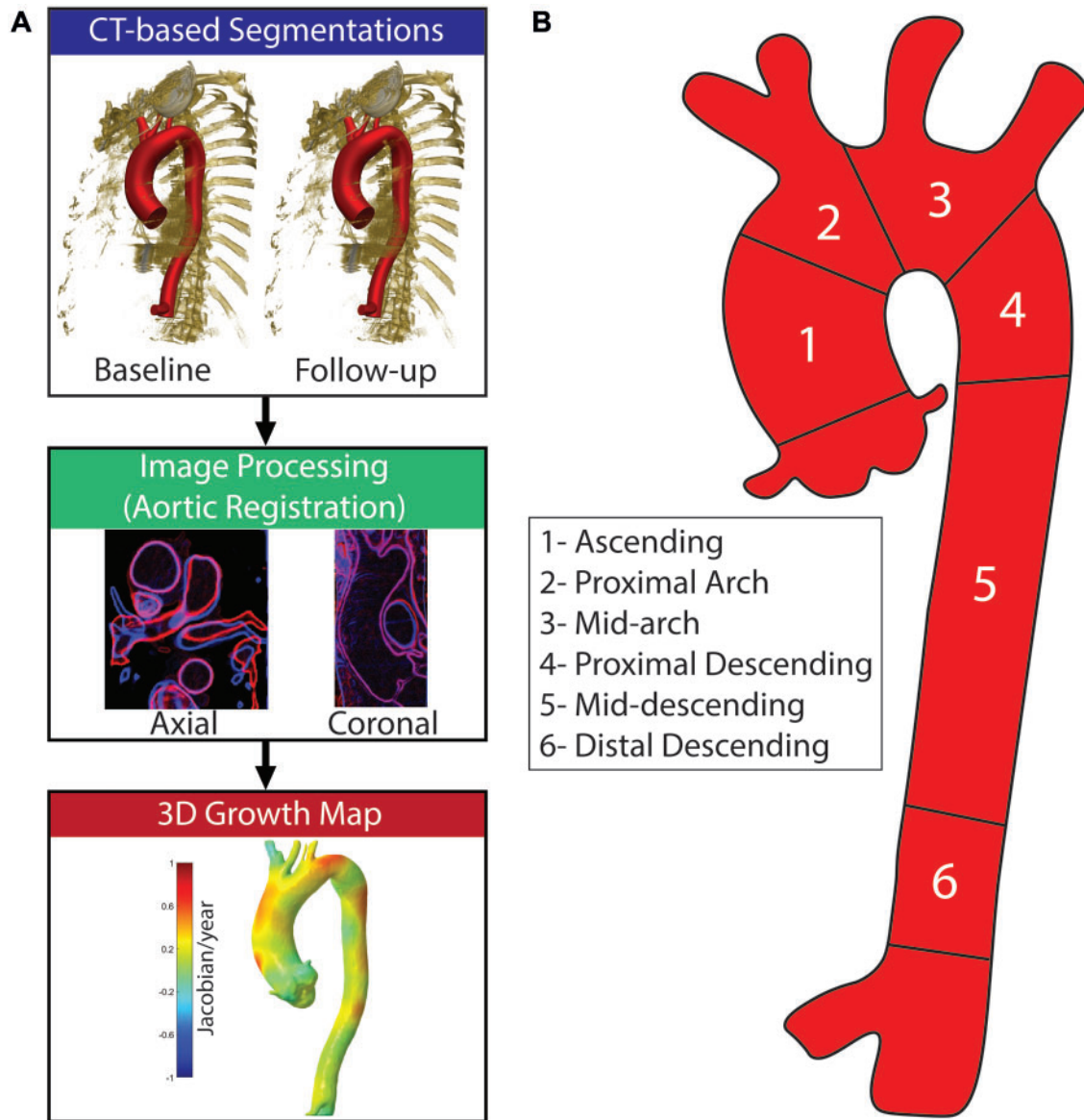


Figure 2: Schematic representation of the steps involved in the vascular deformation mapping analysis (**A**), and the definition of the 6 aortic segments used for analysis of growth (**B**). (1) Ascending aorta: sinotubular junction to superior border of right pulmonary artery, (2) Proximal Arch: right pulmonary artery to distal innominate artery, (3) Mid-arch: innominate artery to distal left subclavian artery (LSA), (4) Proximal Descending: LSA to 2 cm distal to LSA, (5) Mid-descending: 2 cm distal to LSA to 10 cm distal to LSA and (6) Distal Descending: 10 cm distal to LSA to coeliac artery. 3D: three-dimensional; CT: computed tomography.

was confirmed by targeted re-measurement in 5 patients (83%). Three representative cases are reported below, with detailed description of the remaining results included in the [Supplementary Material](#).

Patient 1 underwent an aortic root and ascending aorta replacement. Clinical measurements in this patient suggested clear growth at the proximal descending (+7 mm) and to a lesser extent at the mid-descending and distal descending thoracic aorta (+2 and +3 mm, respectively), as shown in Fig. 3A. These areas of clinically reported growth were clearly identified on VDM analysis (max $J=1.5$, corresponding to 0.5J/year) and confirmed by targeted re-measurements in these locations. Furthermore, there was good agreement in growth trends along the length of the aorta between Jacobian volumetric growth (black circles) and our targeted re-measurements (green squares) (Fig. 3B).

Similar to patient 1, patient 5 underwent an aortic root and ascending aorta replacement. Clinical measurements suggested stable aortic dimension (+1.2 mm at the distal descending aorta), as shown in Fig. 4. In agreement, VDM and targeted re-measurements did not detect any confident growth (max $J=1.2$, corresponding to 0.2J/year). There is reasonable agreement in trends between Jacobian volumetric growth (black circles) and our targeted re-measurements (green squares).

Patient 4 underwent a thoraco-abdominal aortic aneurysm repair. Clinical measurements did not suggest any growth (+0.5 and +1.6 mm at the ascending and distal descending, respectively), as shown in Fig. 5A. However, VDM analysis revealed ascending growth (max $J=1.7$, corresponding to 0.6J/year), which was confirmed by targeted re-measurements (+3.0 mm at the ascending aorta). Again, there was good agreement in

trends between Jacobian volumetric growth (black circles) and our targeted re-measurements (green squares), shown in Fig. 5B.

Correlation analyses and agreement of growth assessment between techniques

Three-dimensional growth measurements revealed good agreement between raters (bias 0.031 J, limits of agreement -0.273–0.335 J), as shown in the [Supplementary Material](#). The mid-arch location in patient 3 was considered an outlier (J = 4.0, diameter growth 8–9 mm) and was excluded from bivariate correlation analysis to avoid disproportionate effects of this single

outlier on the correlation coefficient. We found a weak but statistically significant correlation between volumetric Jacobian measurements and targeted diameter re-measurements ($r = 0.20$; $P = 0.047$; 95% CI: 0.003 to 0.390), but no significant correlation with clinical measurements ($r = 0.15$; $P = 0.141$; 95% CI: -0.051 to 0.343), as depicted in Fig. 6. Additionally, there was a weak-moderate correlation of diameter change as measured by clinical and targeted re-measurements ($r = 0.42$; $P < 0.001$; 95% CI: 0.227 to 0.563). Among the 20 segments with aortic growth by VDM assessment, growth was confirmed in 7 (35%) segments by clinical measurement and 11 (55%) segments in targeted re-measurements. Conversely, among the 18 segments with aortic growth by clinical measurements, growth was confirmed in 7 (39%) segments by VDM and 11 (61%) segments in targeted re-measurements. Binary growth assessments showed greater agreement between volumetric measurements and targeted diameter measurement ($\kappa = 0.38$; $P < 0.001$; 95% CI: 0.139 to 0.617) than with clinical measurements ($\kappa = 0.25$; $P = 0.007$; 95% CI: 0.008 to 0.492) in the aorta overall. When dividing the aorta into a proximal segment (ascending segments 1 and 2) and distal segment (arch and descending segments 3–6), we found low and non-significant agreement between 3D growth and diameter measurements at the proximal segments (targeted measurements: $\kappa = 0.15$, $P = 0.186$; clinical measurements: $\kappa = 0.06$, $P = 0.371$), but moderate and significant agreement at the distal segments (targeted measurements: $\kappa = 0.56$, $P < 0.001$; clinical measurements $\kappa = 0.31$, $P = 0.006$).

DISCUSSION

Our results demonstrate the feasibility of VDM—a tool for 3D aortic growth assessment—in assessing aortic growth in patients undergoing imaging surveillance following open repair of the thoracic aorta. VDM was able to clearly depict the presence or absence of localized aortic growth and allows for a better visual

Table 1: Patient demographics

Variable	Overall (n = 130)	Included (n = 16)
Age, mean \pm SD	60 \pm 12	64 \pm 10
Sex		
Female, n (%)	40 (31)	5 (31)
Male, n (%)	90 (69)	11 (69)
Surgery type		
Ascending (+arch) repair, n (%)	64 (49)	6 (38)
Descending repair, n (%)	47 (36)	5 (31)
Concomitant valve surgery, n (%)	9 (7)	2 (13)
Concomitant root surgery, n (%)	10 (8)	3 (19)
Hypertension, n (%)	100 (77)	14 (89)
Diabetes mellitus, n (%)	14 (11)	1 (6)
Tobacco use, n (%)	72 (55)	10 (63)
COPD, n (%)	39 (30)	4 (25)
Coronary artery disease, n (%)	32 (25)	2 (13)
Connective tissue disease, n (%)	6 (5)	0 (0)
Dyslipidaemia, n (%)	87 (67)	12 (75)

COPD: chronic obstructive pulmonary disease.

Table 2: Aortic growth assessment and follow-up

Patient	Max growth (mm)	Aortic segment	3D aortic growth	Jacobian determinant	CT interval (months)	Follow-up (months)	Reintervention
1	7.0	4	Yes	1.5	12.7	62.8	Yes; +6.8 years ^a
2	0.8	6	Yes	1.6	12.2	15.7	No
3	9.0	3	Yes	4.0	18.1	40.3	Yes; +5.9 years ^b
4	1.6	6	Yes	1.7	12.7	17.0	Yes; +1.7 years ^c
5	1.2	6	No	1.2	12.3	15.7	No
6	1.1	5	No	1.2	14.3	16.7	No
7	1.0	1	No	1.2	12.0	15.1	No
8	1.2	4	No	1.2	11.8	14.7	No
9	0.5	4	No	1.2	12.6	19.1	No
10	2.5	4	No	1.2	11.8	24.7	No
11	2.3	2	No	1.1	11.8	14.8	No
12	6.2	4	No	1.2	12.6	15.8	No
13	3.0	5	Yes	1.5	15.2	18.5	No
14	2.6	3	Yes	1.3	18.7	23.3	No
15	2.2	3	No	1.2	12.5	16.9	No
16	4.2	2	No	1.2	12.0	15.0	No

^aThis patient underwent an ascending + total arch replacement with frozen elephant trunk.

^bThis patient underwent a total arch replacement with frozen elephant trunk.

^cThis patient underwent an ascending + arch replacement.

CT: computed tomography.

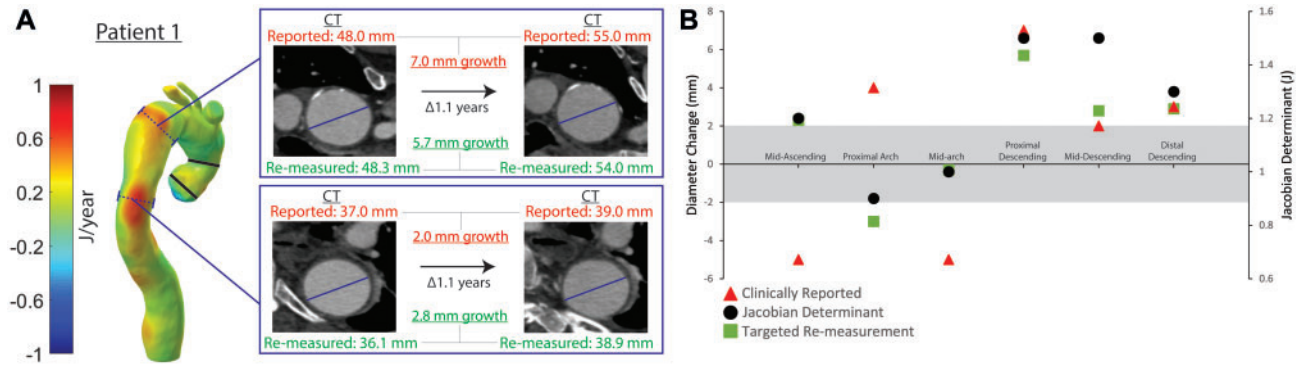


Figure 3: A representative case of an ascending aortic repair case with detected growth (patient 1) is shown with vascular deformation mapping and corresponding diameter measurements (A), as well as comparison of growth measurements along the length of the aorta (B). Grey-shading denotes range of measurements defined as no growth. CT: computed tomography.

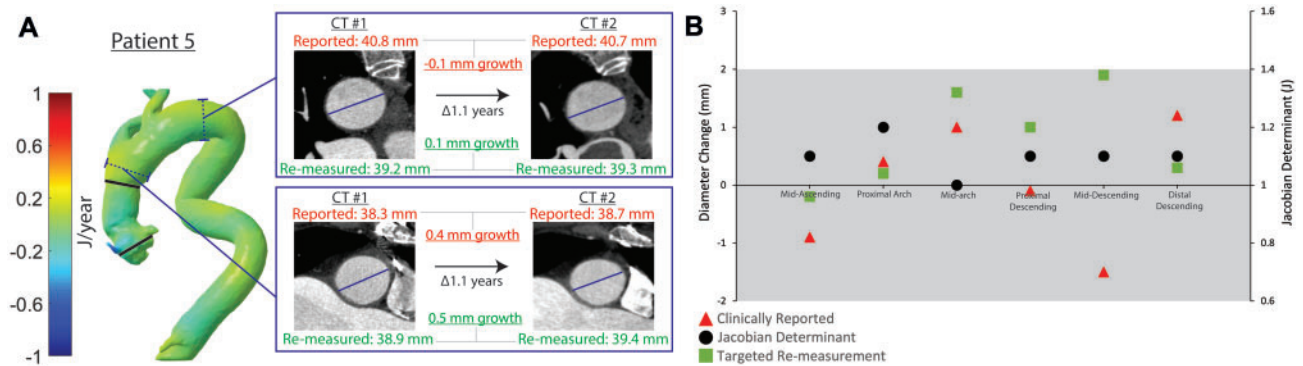


Figure 4: A representative case of an ascending aortic repair without detected growth (patient 5) is shown with corresponding vascular deformation mapping and corresponding diameter measurements (A), as well as comparison of growth measurements along the length of the aorta (B). Grey-shading denotes range of measurements defined as no growth. CT: computed tomography.

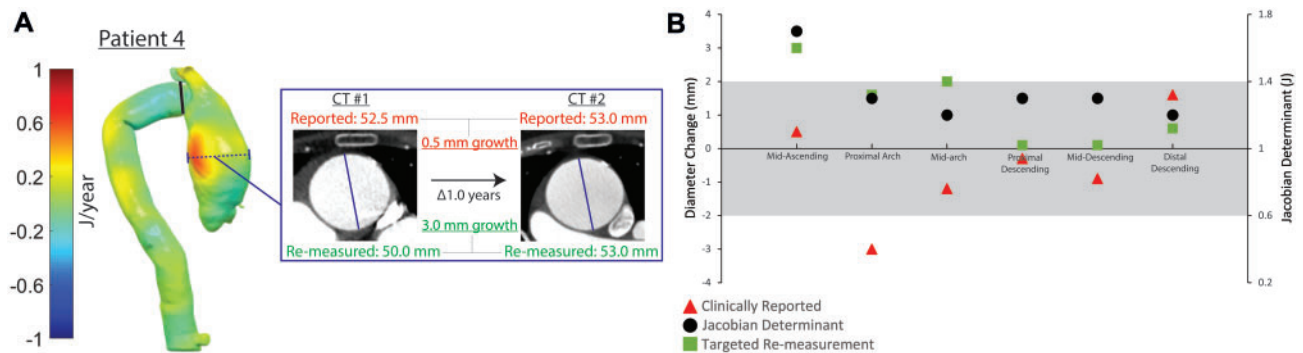


Figure 5: A representative case of a descending thoracic aortic repair with detected growth (patient 4) is shown with corresponding vascular deformation mapping and corresponding diameter measurements (A), as well as comparison of growth measurements along the length of the aorta (B). Grey-shading denotes range of measurements defined as no growth. CT: computed tomography.

representation of the distribution of aortic growth and its relation to anatomic landmarks (e.g. anastomoses, branch arteries), than can be gleaned from standard two-dimensional (2D) diameter measurements. Agreement of growth assessments between VDM and diameter measurements was slightly higher for targeted re-measurements ($\kappa = 0.38$) compared to clinical measurements ($\kappa = 0.25$), and was lowest at the ascending aorta. Furthermore, when analysing the degree of measured aortic growth, we identified a weak but statistically significant correlation between the degree of volumetric growth (J) and the

degree of diameter growth (mm) by targeted re-measurements. We believe these results highlight the potential additive/complementary role of 3D growth mapping in patients undergoing aortic imaging surveillance with standard diameter-based aortic measurement techniques.

A fundamental challenge with aortic surveillance—further highlighted in our study—is the substantial variability of diameter measurements leading to inconsistent or uncertain growth assessments. Aortic diameter measurement variability is typically on the order of ± 2 mm, however, studies on this topic have

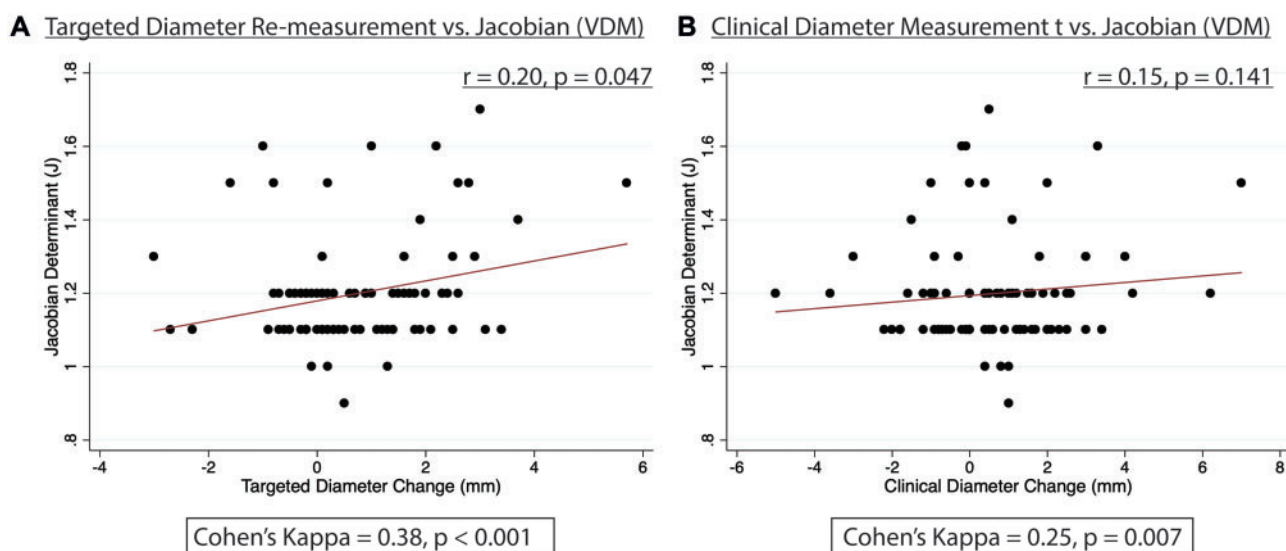


Figure 6: Correlation analysis and agreement of growth assessment between vascular deformation mapping Jacobian-based assessment and targeted re-measurement (A) and clinical measurements (B). VDM: vascular deformation mapping.

demonstrated that measurement discrepancies up to 7–9 mm in magnitude are not uncommon [6, 9, 10]. While this limitation is not unique to the postoperative setting, altered postoperative anatomy due to the presence of a synthetic graft, abrupt diameter changes at anastomoses and the potential for accentuated angulation/tortuosity act to only further exacerbate measurement variability. VDM is a recently developed analysis technique that allows for a 3D assessment of aortic growth and can thus avoid variability in aortic growth measurements related to differences in the position/angulation of the 2D diameter measurement plane. Furthermore, VDM is based on 3D image registration techniques that display measurement errors in the sub-millimetre range, substantially lower than the errors of diameter measurements, and registration errors for VDM are in the range of 0.2–0.6 mm based on results of our technical validation work [11].

While VDM allows for more accurate growth measurement compared to aortic diameter, 1 drawback to the VDM technique is that it is intrinsically difficult to directly compare 3D Jacobian volumetric growth with variable 2D diameter measurements, which may partially explain the weak correlations between these metrics we observed in this study. Further complicating direct comparison of VDM and diameter measurements is the fact that VDM—by its volumetric nature—captures growth in all directions (i.e. radial, longitudinal and circumferential), whereas standard diameter measurements only measure aortic expansion in the radial direction. Nonetheless, a 3D growth assessment may add unique information about disease progression considering the complex 3D structure of the elastic and collagen fibres that provide structural integrity to aortic wall [12]. Further supporting the potential clinical value of a multi-dimensional growth assessment, recent studies have described the value of aortic elongation and subsequent angulation in estimating the risk of adverse aortic events [13, 14]. Finally, there is a crucial distinction to be made between detected growth, defined in this study as any change >2 mm, and clinically relevant growth prompting intervention or strict imaging follow-up, which would arguably be defined as change ≥ 5 mm. Future research should include larger studies with long-term outcomes and focus on assessing the

clinical applicability of VDM and determine the added value of 2D versus 3D growth assessments.

Recent studies have advocated for an imaging surveillance regime tailored to the specific disease, which is reflected in the guidelines (e.g. more stringent follow-up to be considered in acute aortic syndrome) [1–3, 15–17]. Such disease-specific surveillance strategies are based on differential risk of disease progression with each pathology. In this study, 13 patients underwent surgery for aneurysm and 3 patients underwent surgery for dissection, of which 1 patient had an intramural hematoma (IMH) variant type A dissection. The patient who had repaired type A IMH (patient 3) did display the highest degree of postoperative growth in the distal peri-anastomotic region; however, being only a single case, the significance of this finding is uncertain. Otherwise, we did not encounter significant differences in VDM growth patterns in the native aorta between aneurysm and dissection patients in our analysis; however, none of the repaired dissection patients had residual dissections in the evaluated segments. With the advent of techniques for 3D growth assessment (VDM), a similar risk-tailored surveillance approach could be envisioned that relies on an accurate assessment of the presence or absence of aortic growth. Considering that two-thirds of patients in this study (10/16) showed no growth on 3D growth assessment, such patients could likely be spared frequent imaging follow-up.

Reoperation rate after open proximal aortic repair has been reported to be $<5\%$, with median time to reoperation of ~ 3 –5 years [3, 16]. Reinterventions following descending thoracic aortic and thoraco-abdominal repair are more common (13–22%), predominantly due to failure of repair or disease progression of the native aorta [18–20]. Post-surgical aortic growth can present in a peri-anastomotic location, as seen in patient 3, or can affect aortic segments remote to the surgical repair, especially when the unrepaired segment is aneurysmal, as demonstrated most clearly in patients 1, 2 and 4. Given such heterogeneity, aortic growth may be missed by current diameter-based approaches, especially when slow or occurring in areas of distorted post-surgical anatomy. Among the 20 aortic segments in this study with growth detected by VDM, only 7 of these

segments demonstrated growth by clinically reported measurements, highlighting the potential additive value of a 3D assessment. While not specifically addressed in this study, the 3D nature of the VDM growth assessment also allows for closer integration with other advanced aortic assessment techniques such as four-dimensional flow magnetic resonance imaging and computational modelling, and a recent study suggested the potential of a combined analytical approach for predicting the location of entry tear formation in type B aortic dissection using VDM in combination with computation wall stress modelling techniques [21].

Despite demonstrating feasibility of our approach, these results are limited by the small sample size and heterogeneity of aortic pathology. Future efforts will focus on investigating 3D growth assessment techniques in larger cohorts to better understand the ability of a postoperative 3D growth analysis to predict future complications, refine risk assessment and tailor imaging surveillance frequency. As this study is limited to patients that underwent open surgical repair, assessment of aortic growth following endovascular repair (TEVAR) could represent the topic of future research. Patients with connective tissue disease were not included in our analysis. Given their intrinsically higher risk of aneurysmal degeneration, we believe future research should focus on assessing 3D growth in these patients. Similarly, we plan to assess potential growth differences between aneurysm and dissection patients with residual dissections. Additionally, given the 3D nature of VDM, we plan future studies to investigate the role of isolated radial and longitudinal aortic growth assessments.

Limitations

There are several limitations to this study. First, by selecting a subgroup of patients out of a larger surgical population in which to test feasibility, there is potential for selection bias. However, we did not encounter any notable differences when comparing the analysed cohort to excluded patients, suggesting that the analysed cohort is representative of our overall surgical population. A comprehensive assessment of the diagnostic performance of diameter measurements versus VDM in larger cohorts is the subject of ongoing research efforts. Second, because the VDM technique relies on high-fidelity CTA data it is subject to potential errors when image artefacts related to motion or streaking are present. This limitation may in part explain why agreement between 3D growth and diameter assessments was lowest in the ascending aorta where artefacts are more common. Furthermore, while the VDM technique has been validated using experimental phantoms, there is no ground-truth method of verifying 3D growth assessments in clinical cases. However, in this study, we employed stringent CTA data quality checks and a multi-step quality assurance process to ensure the accuracy of CTA registration and minimize the potential for erroneous VDM outputs. Additionally, VDM analysis currently requires more time than standard diameter measurements (~20 min per segmentation and 10 min for registration); however, technical work is currently underway to significantly reduce the segmentation time through the use of machine learning techniques. Third, the single-centre nature of this study does not allow for assessment of the reproducibility of the VDM workflow, which includes operator learning curve, image quality selection and application of the measurement protocol.

CONCLUSION

In conclusion, aortic growth is often underappreciated when assessed via 2D diameter measurements. Three-dimensional growth of the native aorta after open thoracic aortic repair was varied in intensity and distribution, occurring in areas close to and remote to the surgical margins. Three-dimensional growth assessment with VDM can help overcome challenges of diameter measurement variability, offers a complete growth assessment over the entire aortic wall and allows for targeted diameter measurements in areas of suspected growth. VDM is a promising technique to allow for more accurate definition of post-surgical patients at high and low risk for future complications.

SUPPLEMENTARY MATERIAL

Supplementary material is available at *EJCTS* online.

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Author contributions

Yunus Ahmed: Conceptualization; Data curation; Formal analysis; Investigation; Methodology; Project administration; Resources; Validation; Visualization; Writing—original draft; Writing—review & editing. **Nitesh Nama:** Conceptualization; Formal analysis; Investigation; Methodology; Resources; Software; Validation; Writing—review & editing. **Ignas B. Houben:** Conceptualization; Investigation; Methodology; Writing—review & editing. **Joost A. van Herwaarden:** Conceptualization; Supervision; Writing—review & editing. **Frans L. Moll:** Conceptualization; Supervision; Writing—review & editing. **David M. Williams:** Conceptualization; Supervision; Writing—review & editing. **C. Alberto Figueroa:** Conceptualization; Funding acquisition; Methodology; Resources; Software; Supervision; Writing—review & editing. **Himanshu J. Patel:** Conceptualization; Funding acquisition; Methodology; Resources; Supervision; Writing—review & editing. **Nicholas S. Burris:** Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Resources; Software; Supervision; Validation; Visualization; Writing—original draft; Writing—review & editing.

Reviewer information

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REFERENCES

- [1] Erbel R, Aboyans V, Boileau C, Bossone E, Di BR, Eggebrecht H *et al.* 2014 ESC guidelines on the diagnosis and treatment of aortic diseases. *Eur Heart J* 2014;35:2873–926.
- [2] Hiratzka LF, Bakris GL, Beckman JA, Bersin RM, Carr VF, Casey DE, Society for Vascular Medicine *et al.* 2010 ACCF/AHA/AATS/ACR/ASA/SCA/SCAI/SIR/STS/SVM Guidelines for the diagnosis and management of patients with thoracic aortic disease. *Anesth Analg* 2010;111:279–315.
- [3] Iribarne A, Keenan J, Benrashed E, Wang H, Meza JM, Ganapathi A *et al.* Imaging surveillance after proximal aortic operations: is it necessary? *Ann Thorac Surg* 2017;103:734–41.
- [4] Park CB, Greason KL, Suri RM, Michelena HI, Schaff HV, Sundt TM. Should the proximal arch be routinely replaced in patients with bicuspid aortic valve disease and ascending aortic aneurysm? *J Thorac Cardiovasc Surg* 2011;142:602–7.
- [5] Reece TB, Aftab M. Invited commentary. *Ann Thorac Surg* 2018;106:776–7.
- [6] Quint LE, Liu PS, Booher AM, Watcharotone K, Myles JD. Proximal thoracic aortic diameter measurements at CT: repeatability and reproducibility according to measurement method. *Int J Cardiovasc Imaging* 2013;29:479–88.
- [7] Burris NS, Hoff BA, Kazerooni EA, Ross BD. Vascular deformation mapping (VDM) of thoracic aortic enlargement in aneurysmal disease and dissection. *Tomography* 2017;3:163–73.
- [8] Burris NS, Hoff BA, Patel HJ, Kazerooni EA, Ross BD. Three-dimensional growth analysis of thoracic aortic aneurysm with vascular deformation mapping. *Circ Cardiovasc Imaging* 2018;11:e008045.
- [9] Müller-Eschner M, Rengier F, Partovi S, Weber TF, Kopp-Schneider A, Geisbüsch P *et al.* Accuracy and variability of semiautomatic centerline analysis versus manual aortic measurement techniques for TEVAR. *Eur J Vasc Endovasc Surg* 2013;45:241–7.
- [10] Lu TLC, Rizzo E, Marques-Vidal PM, Von Segesser LK, Dehmeshki J, Qanadli SD. Variability of ascending aorta diameter measurements as assessed with electrocardiography-gated multidetector computerized tomography and computer assisted diagnosis software. *Interact CardioVasc Thorac Surg* 2010;10:217–21.
- [11] Klein S, Staring M, Pluim JPW. Evaluation of optimization methods for nonrigid medical image registration using mutual information and B-splines. *IEEE Trans Image Process* 2007;16:2879–90.
- [12] Tsamis A, Krawiec JT, Vorp DA. Elastin and collagen fibre microstructure of the human aorta in ageing and disease: a review. *J R Soc Interface* 2013;10:20121004.
- [13] Wu J, Zafar MA, Li Y, Saeyeldin A, Huang Y, Zhao R *et al.* Ascending aortic length and risk of aortic adverse events: the neglected dimension. *J Am Coll Cardiol* 2019;74:1883–94.
- [14] Gode S, Akinci O, Ustunisk CT, Sen O, Kadirogullari E, Aksu T *et al.* The role of the angle of the ascending aortic curvature on the development of type A aortic dissection: ascending aortic angulation and dissection. *Interact CardioVasc Thorac Surg* 2019;29:615–20.
- [15] Bilkhu R, Youssefi P, Soppa G, Theodoropoulos P, Phillips S, Liban B *et al.* Fate of the aortic arch following surgery on the aortic root and ascending aorta in bicuspid aortic valve. *Ann Thorac Surg* 2018;106:771–6.
- [16] Estrera AL, Miller CC, Porat E, Mohamed S, Kincade R, Huynh TT *et al.* Determinants of early and late outcome for reoperations of the proximal aorta. *Ann Thorac Surg* 2004;78:837–45.
- [17] Estrera AL, Miller CC, Villa MA, Lee TY, Meada R, Irani A *et al.* Proximal reoperations after repaired acute type A aortic dissection. *Ann Thorac Surg* 2007;83:1603–9.
- [18] Coselli JS, Rosu C, Amarasekara HS, Green SY, Zhang Q, Price MD *et al.* Reoperative surgery on the thoracoabdominal aorta. *J Thorac Cardiovasc Surg* 2018;155:474–85.e1.
- [19] Carrel T, Pasic M, Jenni R, Tkebuchava T, Turina MI. Reoperations after operation on the thoracic aorta: etiology, surgical techniques, and prevention. *Ann Thorac Surg* 1993;56:259–69.
- [20] Bekkers JA, Te Riele RJLM, Takkenberg JJM, Bol Raap G, Hofland J, Roos-Hesselink JW *et al.* Thoracic aortic surgery: an overview of 40 years clinical practice. *J Thorac Cardiovasc Surg* 2014;147:332–43.
- [21] Houben IB, Nama N, Moll FL, van Herwaarden JA, Nordsletten DA, Williams DM *et al.* Mapping pre-dissection aortic wall abnormalities: a multiparametric assessment. *Eur J Cardiothorac Surg* 2020;57:1061–7.