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On growth measurements of abdominal aortic aneurysms using maximally inscribed spheres

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ABSTRACT

The maximum diameter, total volume of the abdominal aorta, and its growth rate are usually regarded as key factors for making a decision on the therapeutic operation time for an abdominal aortic aneurysm (AAA) patient. There is, however, a debate on what is the best standard method to measure the diameter. Currently, two dominant methods for measuring the maximum diameter are used. One is measured on the planes perpendicular to the aneurism's central line (orthogonal diameter) and the other one is measured on the axial planes (axial diameter). In this paper, another method called 'inscribed-spherical diameter' is proposed to measure the diameter. The main idea is to find the diameter of the largest sphere that fits within the aorta. An algorithm is employed to establish a centerline for the AAA geometries obtained from a set of longitudinal scans obtained from South Korea. This centerline, besides being the base of the inscribed spherical method, is used for the determination of orthogonal and axial diameter. The growth rate parameters are calculated in different diameters and the total volume and the correlations between them are studied. Furthermore, an exponential growth pattern is sought for the maximum diameters over time to examine a nonlinear growth pattern of AAA expansion both globally and locally. The results present the similarities and discrepancies of these three methods. We report the shortcomings and the advantages of each method and its performance in the quantification of expansion rates. While the orthogonal diameter measurement has an ability of capturing a realistic diameter, it fluctuated. On the other hand, the inscribed sphere diameter method tends to underestimate the diameter measurement but the growth rate can be bounded in a narrow region for aiding prediction capability. Moreover, expansion rate parameters derived from this measurement exhibit good correlation with each other and with growth rate of volume.

In conclusion, although the orthogonal method remains the main method of measuring the diameter of an abdominal aorta, employing the idea of maximally inscribed spheres provides both a tool for generation of the centerline, and an additional parameter for quantification of aneurysmal growth rates.

1. Introduction

An abdominal aortic aneurysm (AAA) is the localized enlargement of the abdominal aorta that affects a large part of the elderly population; and the more it dilates, the more it will become prone to rupture that is associated with a high mortality rate. Current treatments involve surgical, and either open or endovascular repair. Unfortunately, the risk of these approaches is also high. Therefore, there is an imperative need to decide whether or not an AAA patient needs a medical intervention. Nonetheless, there is no solid argument regarding the appropriate time for an AAA patient to undergo surgery [1–3]. In clinical practice, aneurysms with diameters larger than 50 or 55 mm are considered for surgical intervention [4–10]. There are, however, uncertainties about the methods of measurement of the diameter [11–14], quantification of dynamic factors [2,15,16], and even sufficiency of the diameter as a predictor for AAA size evolution [1,3,15–19]. These uncertainties have led others to suggest other parameters: the AAA volume, blood pressure, age, sex, and calcium level as predictors for the time of surgery for AAA patients [1–3, 20–22].

Previous studies have utilized various ways of measuring the maximum diameter of an AAA and its growth rate. Although investigators have suggested different methods, most of them involve finding

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the maximum diameter either on an axial plane ("axial diameter") or on a plane orthogonal to aorta's centerline ("orthogonal diameter") [12,13,16,21,23,24]. Major concerns associated with measuring the diameter are, however, the accuracy of the estimation and reproducibility of the method [13]. Abada et al. [11] recommended using the maximum anterior posterior or maximum transverse diameter on axial slices. Dugas et al. [13] studied differences of the axial and orthogonal diameter measurements and suggested that the axial diameter measurements overestimate the diameter and that the orthogonal diameter method is more reproducible. Kontopodis et al. [12] illustrated that the median of the differences between the two methods are not high but there are cases where the wide range of differences in measurement possibly affect therapeutic decisions. Those studies proposed that the orthogonal diameter can better represent the AAA size than the axial diameters do, while finding that the perpendicular plane to vessel centerline can result in measurement uncertainty.

Volume has been introduced as an alternative factor to assess aneurysm development in an AAA patient [2,12,15,16,18,25,26]. Raghavan et al. [26] have reported that AAA volume and rupture risk are correlated more strongly than diameter and rupture risk. In their study, to calculate the total volume of an AAA, the aneurysm is axially sliced and the cross sectional area of each axial slice is multiplied by the vertical distance between the centroids of two consecutive slices. Kleinstreuer and Li [2] proposed a severity parameter that integrates alterations of different biomechanical factors (such as maximum diameter and expansion rate) over time by a single value. Recently, Martufi et al. [16] suggested that monitoring only the maximum diameter for surveillance programs may wrongly reflect the expansion related to wall weakening. In their paper, centerline based tools have been introduced to compare the suitability of localized and global parameters. They claimed that monitoring localized spots of fast diameter growth might greatly enhance the efficiency of AAA surveillance programs. Additionally, growth of AAAs is measured by means of an exponential growth model. However, computing growth is somewhat of a subjective issue among researchers.

There are simple ways, of course, to define growth rates in different AAA size measurements (cf. [15] and [16]). One approach is quantifying the growth rate by calculating the change in the diameter divided by the time interval between two consecutive images in a linear fashion. Nonetheless, there are multiple practical issues associated with this method such as an inaccuracy due to a relatively small change in diameter over time, the nonlinear nature of the expansion [27], and so forth. Several studies have utilized an exponential growth function for predicting AAA expansion over time [15,16,21,28–30]. Although Martufi's study [16] suggested that an exponential growth parameter can capture AAA's growth, more studies need to be conducted to increase our understanding of an AAA growth pattern; hence, one of the objectives of this study is to examine whether the exponential growth pattern is reasonable so that it can provide a prediction capability for AAA clinical management.

The present study also introduces a new method for the AAA's diameter measurement. This method involves finding the diameters of maximally-inscribed spheres within the geometry, and consequently constructing the centerline using the series of spheres' centers. This idea has been widely used for different purposes among researchers [31–33]. We suggest that the proposed definition of the diameter carries useful information related to the size of the AAA, which can be used along with other methods to find the correlations among different geometric parameters and their growth rates. Additionally, this method possibly assists in prediction of the future progression of the disease.

To this end, an efficient computational algorithm is developed to compute the inscribed-spherical diameter, and the advantages of using this method are presented. Besides, an exponential growth pattern for maximum diameter is evaluated in the patient group.

2. Methods

2.1. Exponential growth rate

An exponential growth model is a widely accepted growth rate for many biological and physical occurrences. The growth model is proposed based on a nonlinear growth rate g introduced in [16].

$$g = \left(\mathrm{Exp}\,(12r) - 1\right) \times 100\ [\%/\mathrm{year}] \tag{1}$$

where the variable r is measured using a logarithmic growth rate

$$r = \frac{1}{t}\ln\left(\frac{X^{\mathrm{follow-up}}}{X^{\mathrm{baseline}}}\right). \tag{2}$$

The quantity X is measured and t is the time interval between two consecutive images in months. To calculate the logarithmic growth rate, the two quantities, $X^{\mathrm{follow-up}}$ and X^{baseline}, are at the same position on the normalized centerline.

Eq. (1) combined with Eq. (2) can be rewritten for the maximum diameter D as below

$$D^{\mathrm{follow-up}} = D^{\mathrm{baseline}}\left(1 + \frac{g}{100}\right)^{\frac{t}{12}}. \tag{3}$$

It is equivalent to the following form:

$$D^{\mathrm{follow-up}} = D^{\mathrm{baseline}} e^{kt} \tag{4}$$

where

$$k = \ln\left(1 + \frac{g}{100}\right)\Big/12. \tag{5}$$

Using these equations, an exponential function can provide a curve representing the evolution of the maximal diameter versus time for all the patients. Since the first scan time on monitoring the disease progression of the patients is not the same, each set of data is unfixed with respect to time, without changing the time intervals between two successive images. However, the values measured for diameters are maintained the same. An initial curve is then chosen and the patient's data are moved to match the exponential curve using the least square method. Then another curve is fitted and the process continues iteratively until a certain minimum amount of error is reached. This general exponential curve can be employed to achieve a better understanding of an AAA size and a more accurate prediction of the evolution of the disease.

2.2. CT scan data

This study was subject to Internal Review Board approvals at Michigan State University and Seoul National University Hospital.

A total of 59 computed tomography (CT) scan data for 14 AAA patients were obtained from Seoul National University Hospital, South Korea. Patients were scanned repeatedly between 3 and 56 months, and the median was 8 months for all of the follow-up periods. The scans were performed using a 100 kV, 88 mA s Somatom Sensation 16 CT scanner (Siemens Healthcare, Erlangen, Germany). The slice thickness is 1 mm and 2D pixel size is 0.641 mm. Further information about the patients is presented in Table 1.

2.3. Maximally inscribed sphere diameters

A biomedical software, MIMICS® (Materialize, Leuven, Belgium), is used to reconstruct segmented 3D longitudinal CT data. A smoothing operation is performed after segmentation to sooth down the roughness of the surface resulted from automatic segmentation.

Three-dimensional point clouds for the AAA wall with iliac arteries are acquired from the software as an embodiment of the volume of the abdominal aorta (Fig. 1). The point cloud model is essentially a subset of a stereo-lithography (STL) model constructed solely of the vertices of the STL model, which is comprised of four surfaces: two

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Table 1
Patients' demographics for AAAs. The age is the time at which the first scan was taken.

Patient ID	Number of scans	Age	Gender
P01	2	68	M
P02	3	71	M
P03	2	69	M
P04	3	63	F
P05	5	65	M
P06	7	68	M
P07	6	66	M
P08	5	54	M
P09	5	62	M
P10	4	73	M
P11	4	59	M
P12	6	70	M
P13	4	54	M
P14	3	72	M

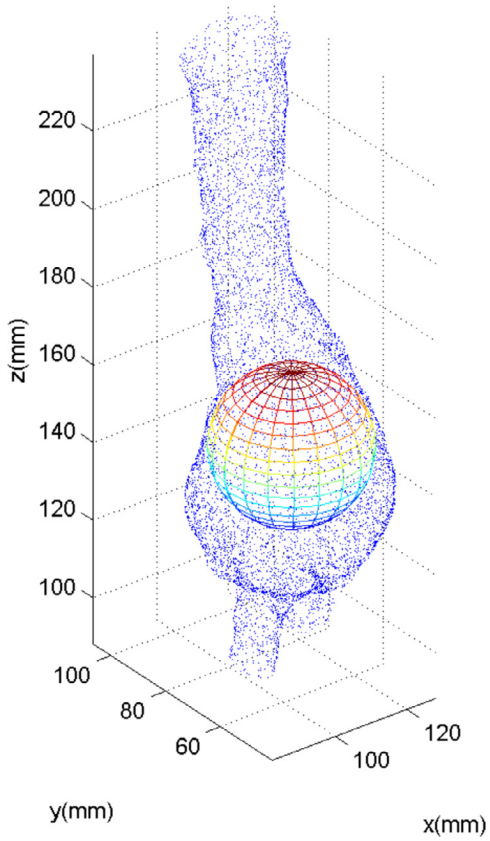

Fig. 1. A schematic drawing for illustrating a set of clouded points for the 3D model of an AAA and a maximally inscribed sphere.

iliac outlet surfaces, one inflow surface at renal level, and the outer wall surface of the abdominal aorta model.

A centerline is a smooth approximation of an infinite series of spherical center points, wherein a maximally inscribed sphere is the largest sphere within the outer arterial wall surface at a centerline point (Fig. 1; [34]). The algorithm of this centerline generation begins by using the centroid of one of the outlet planes as an initial center point guess. Afterwards, the distance from the nearest point in the point cloud and the initial point is computed and the vector connecting these two points is saved. The center of the sphere then moves in the opposite direction of this vector on the outlet plane, within a fixed distance δs. During the iteration, the position of the centerline is decided when the next position does not change over 15 iterations. When this process is complete, the first center point (p_1) is recorded. For the second point (p_2) we proceed a fixed distance in the direction normal to the outlet plane and repeat the algorithm described previously.

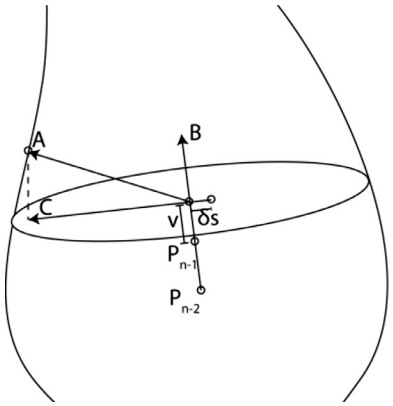

Fig. 2. Schematic drawing of procedure of finding the nth center point.

Using the previous two successive points, the normal direction $B = p_{n-1} - p_{n-2}$ is calculated and serves as an initial translation direction. The new center point translates by B with the magnitude v. When the distance from p_n to the point on the surface (point cloud) is the minimum value from all points, the vector from p_n to this nearest point is calculated and denoted by A, shown in Fig. 2. The vector C is defined by the projection of A onto the plane normal to B

$$C = A - \frac{A \cdot B}{||B||^2} B. \tag{6}$$

The center point p_n is then translated in the opposite direction of C by δs. The iterative process continues and the estimated point keeps translating on the plane (normal to B). The final p_n is determined when the point has not changed by 1 mm over 15 iterations, and then the algorithm starts again for the next center point. Using the sphere center points and polynomials of fourth order as base functions, a smooth line approximation as a centerline is made. After the centerline is generated, the two bottom cut-planes are determined when the centerlines of two iliac arteries meet at the iliac bifurcation, in which two iliacs are cut normal to their centerlines. Similarly, by using the plane normal to the centerline, the upper cut-plane is determined at the lowest renal level. The algorithm is insensitive to the choice of the chosen outlet cut planes.

An orthogonal plane is generated normal to the centerline. An orthogonal diameter (D^O) is the maximum diameter, passing through center point, on each orthogonal plane. Similarly, an axial diameter (D^A) is the maximum diameter on each plane in the axial direction. The sphere diameter is defined as the largest diameter (D) of the maximally inscribed spheres within the AAA volume, and the average of diameter along the aorta (D_{mean}) are defined. Using a commercial mesh generation software package for the constructed volume of AAA, the geometry is meshed using tetrahedral elements. The summation of all the volumes of these elements constructs the total volume of the abdominal aortic aneurysm (V) in this work. The extremities of the volume calculation are presented in Fig. 3.

2.4. Growth rate measurements

For the purpose of investigating growth rates in various parameters, the following parameters are employed. Diameter growths are computed at all the center points which are at relatively the same position on the centerline. Fastest and average diameter growth rates over the entire aneurismal sac are denoted by $g_{\max}$ and g_{mean}, respectively. Regarding the appellation for each of diameter measurement methods, growth rates in maximum diameter in inscribed-spherical, orthogonal, and axial diameter are g_D, $g_{D(O)}$, and $g_{D(A)}$. The growth average of diameter is called $g_{D(\text{mean})}$. Finally, the growth rate in total

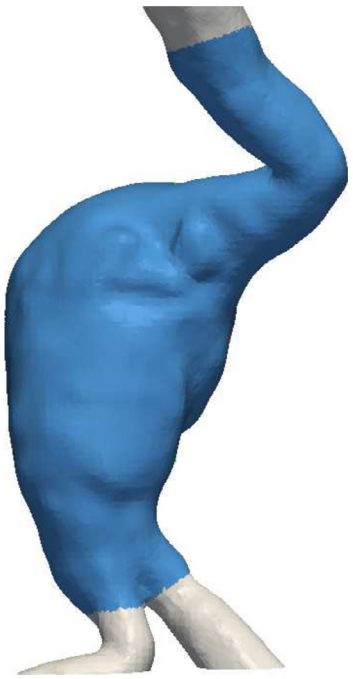

Fig. 3. The bounds of the abdominal aortic aneurysm considered for this study. The iliac branches are cut orthogonal to their respective centerlines.

Table 2
Summary of growth rate parameters.

Parameter	Description
g_{max}	Fastest growth in the diameter measured by the inscribed-spherical diameter
g_{mean}	Average of the growth rate of the diameter measured by the inscribed-spherical diameter
g_D	Growth rate of the maximum diameter using the inscribed-spherical diameter
$g_{D(mean)}$	Growth rate of the average of the diameter using inscribed-spherical diameter
g_V	Growth rate of the aneurysm sac volume
$g_{D(O)}$	Growth rate of the maximum diameter using the orthogonal method
$g_{D(A)}$	Growth rate of the maximum diameter using the axial method
$g_{mean(O)}$	Average of the growth rate of diameter using the orthogonal method
$g_{mean(A)}$	Average of growth rate of the diameter measured by the axial method
$g_{max(O)}$	Fastest growth in diameter measured by the orthogonal method
$g_{max(A)}$	Fastest growth in diameter measured by the axial method

volume is denoted as g_V. The following Table 2 summarizes all the growth rate parameters presented in with a brief description. For the growth rate calculations in the following sections, only the paired scans with the time interval of more than 6 months are used.

A Pearson's correlation r is calculated between all pairs of growth parameters. This analysis was carried out to assess the suitability of different parameters in monitoring the AAA expansion rate. Additionally, median and interquartile ranges (IQR) for growth parameters are calculated. An ANOVA, Shapiro-Wilk tests, and multiple pairwise t-tests are done using R statistical analysis software (v 3.0.2, R Foundation, Vienna, Austria) with the significance level $\alpha = 0.025$. The same significance level is utilized for a correlation study.

3. Results

Using one scan image, the step size v was determined. Individual centerlines were generated with different step sizes and the results

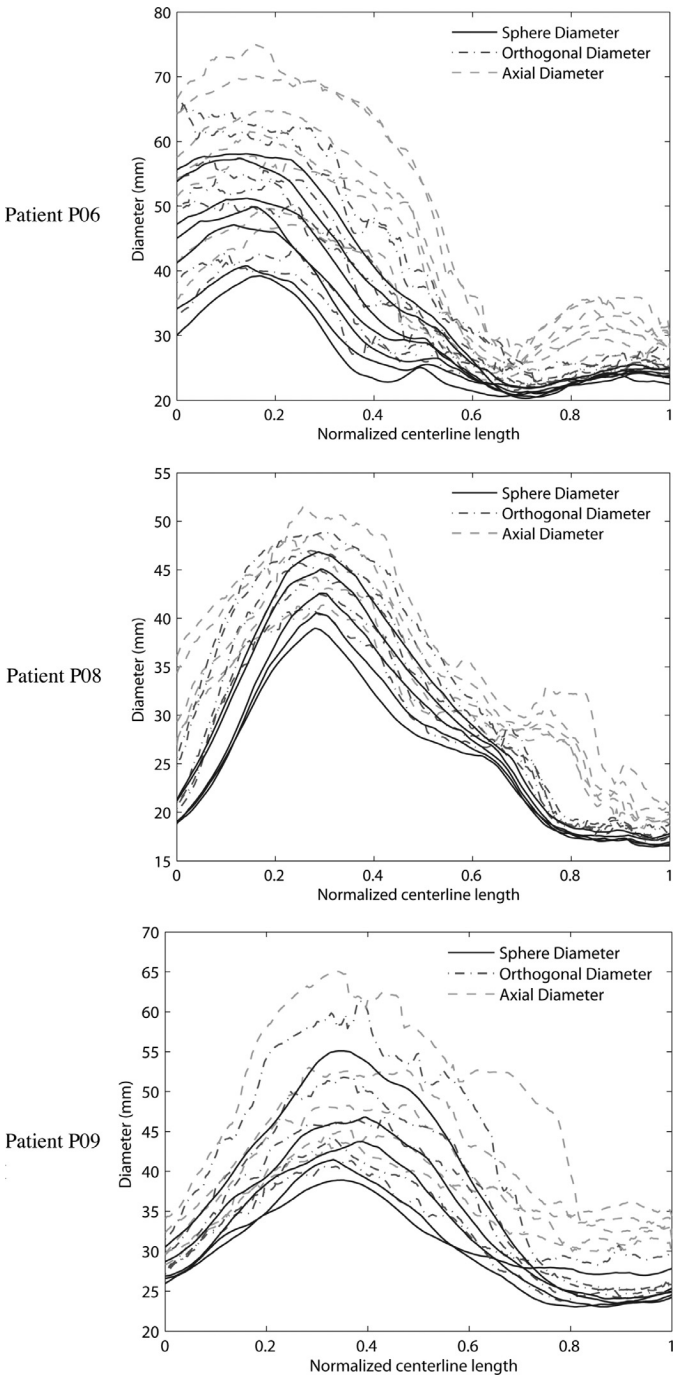

Fig. 4. Orthogonal, axial, and inscribed-spherical diameters over centerline for patients, P06, P08, and P09.

found that the maximum v is 6 mm, below which the path of the centerline almost did not change. Considering the computational costs, a 6 mm of step size is opted for all the study. Regardless, centerline is not sensitive to a higher value of step size. However, for the in-plane step size, δs, of less than 0.05 mm, in which the approximate value is far less than the limit of the CT image resolution, the algorithm becomes instable.

Orthogonal, axial, and inscribed-spherical diameters over a normalized centerline for three patients (P06, P08 and P09) are illustrated in Fig. 4. Using the set of the point clouds for patients' images, all of the different diameter measurements are automatically generated. Clearly, the inscribed-spherical diameter shows a smoother curve in

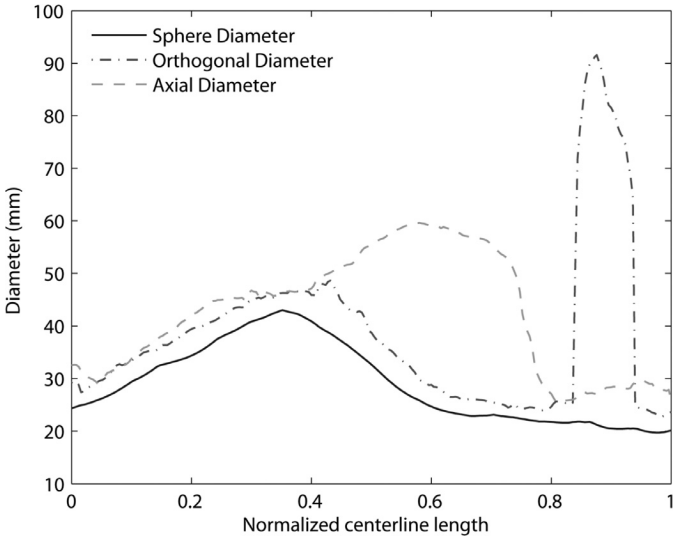

Fig. 5. Three diameter measurements for Patient P02-3. The P02-3 denotes the third scanned image from patient P02 during the follow-up scans at the different times.

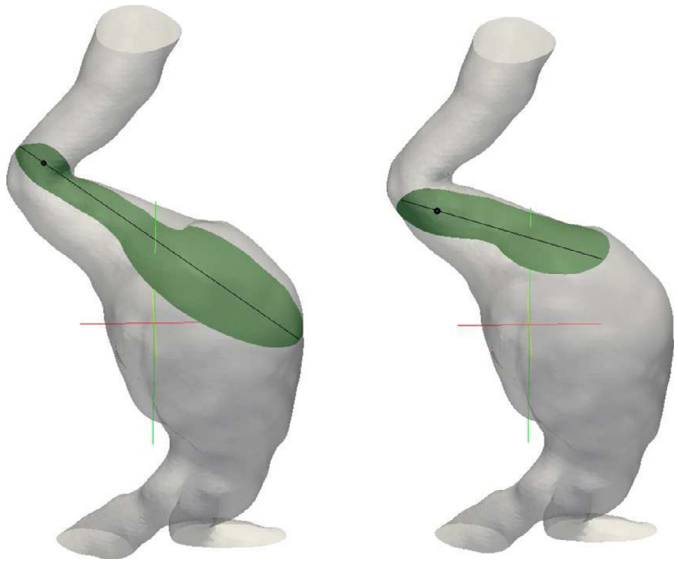

Fig. 6. The left panel shows the cross section on orthogonal plane and the right panel shows the cross section on the axial plane. The black dot is the intersection of the centerline with planes.

comparison with the orthogonal and axial diameters. Also, the plots of the axial diameters show high fluctuations along the normalized centerline length and it appears that the previous plot of the scan can be significantly changed from the next plot. An ANOVA resulted that the difference between maximum diameters measured are different across these three methods. The average and the largest differences between the axial and inscribed-spherical measurements for the maximum diameter among all of the scans are 8 and 18 mm respectively. On the other hand, the difference between the orthogonal and inscribed-spherical measurements for the maximum diameter is on average 4 mm with a maximum of 16 mm. Finally, the maximum values of the axial and orthogonal diameter measurements vary by 3 mm on average and by 15 mm maximally. Both the inscribed-spherical and orthogonal diameters follow similar patterns in these three patients; but the measured values do not coincide, which naturally contributes to discrepancies in later investigations.

The difference between three methods is directly dependent on the shape of the AAA. As an example, for patient P02, the risk of inaccuracy of automatically measuring the diameter using the orthogonal diameter can be observed (Fig. 5). This happens due to an abrupt change in the direction of the centerline where the aneurysmal neck starts to expand (Fig. 6). Similarly, the axial diameter (the marked region shown the right panel of Fig. 5) is erroneously measuring the AAA diameter over the centerline.

An uncertainty analysis is conducted on the orthogonal diameter method to assess the influence of a small error in finding the orthogonal plane on the calculation of the diameter of an AAA. A set of orthogonal planes is chosen along the centerline and then tilted 5° in ten different uniformly discrete directions. The results for the two scans are shown in Fig. 7.

The left panel of Fig. 7 (Patient P08-3) shows relatively low variability to the orthogonal plane selection, in comparison with the right panel of Fig. 7 (Patient P09-3), which displays about a 15 mm misestimation of a maximum orthogonal diameter. Three dimensional models of AAAs shown on the upper right corner of each panel in Fig. 7 illustrate the dependency of the diameter measurement on the shape of the aneurysm.

The total volumes of AAAs and the maximum inscribed spherical diameters are plotted in Fig. 8 for all the patients studied in this paper. A general trend expresses a continuous growth of the diameter and volume over time, while a small amount of contraction in the volume is seen for some of the patients. Interestingly, the aneurysmal volume of Patient P06 remains constant in the first three images, while the diameter keeps on growing; but a large growth abruptly started after the 4th image was observed. It is worth mentioning that the surveillance period is nearly the same between scan 1–3 and scan 3–6 (almost 4 years) for this patient.

Patients P07 and P08, on the other hand, have relatively small changes in volume. Specifically, Patient P07 has one of the smallest AAAs. In addition, the time interval between the third and seventh scan of Patient P06 was approximately 40 months, while Patient P07 was scanned over a period of almost 70 months.

Before presenting the growth rate results, patient P11 was omitted from the statistical analysis due to some irregularities in automatic quantification of orthogonal diameters. A Shapiro-Wilk test on different growth rate parameters confirmed the normality of the data. The computed growth rates in AAA dimensions are depicted in Fig. 9. The growth rate of the maximum diameter g_D (median 5.28%/year, IQR 5.00%/year) is significantly different from the maximum growth rate in diameter g_{max} (median 10.69%/year, IQR 6.61%/year) with p-value$<$0.001. This denotes that the maximum growth does not necessarily coincide with the point of the normalized centerline length where the aneurysm diameter is the maximum. The average growth rate of diameter is g_{mean} (median 3.14%/year, IQR 4.24%/year), which is also different from $g_{D(mean)}$ (median 3.74%/year, IQR 4.18%/year) with p-value$<$0.001. The change in the total volume g_V has the largest range amongst all geometrical properties (median 7.12%/year, IQR 15.60%/year).

The correlation analysis demonstrates that g_V is correlated with $g_{D(mean)}$ ($r = 0.48$, p-value $= 0.005$) and g_{max} ($r = 0.53$, p-value $= 0.0015$), respectively. The correlation between g_{mean} and g_V ($r = 0.40$, p-value $= 0.0205$) is not statistically significant, although the small p-value possibly indicates some weak evidence on the correlation. On the other hand, the correlation between g_V and g_D ($r = 0.53$, p-value $= 0.0015$) is statistically significant based on the p-value. As expected, strong correlations were observed between g_{mean} and g_{max} ($r = 0.70$, p-value < 0.001), g_{mean} and $g_{D(mean)}$ ($r = 0.99$, p-value < 0.001) and g_{mean} and g_D ($r = 0.60$, p-value < 0.001). Furthermore, relatively robust correlations between g_{max} and g_D ($r = 0.75$, p-value < 0.001) and g_{max} and $g_{D(mean)}$ ($r = 0.75$, p-value < 0.001) are observed. These correlations and the rest of important correlations between parameters are summarized in the correlation analysis Table 3 shown below.

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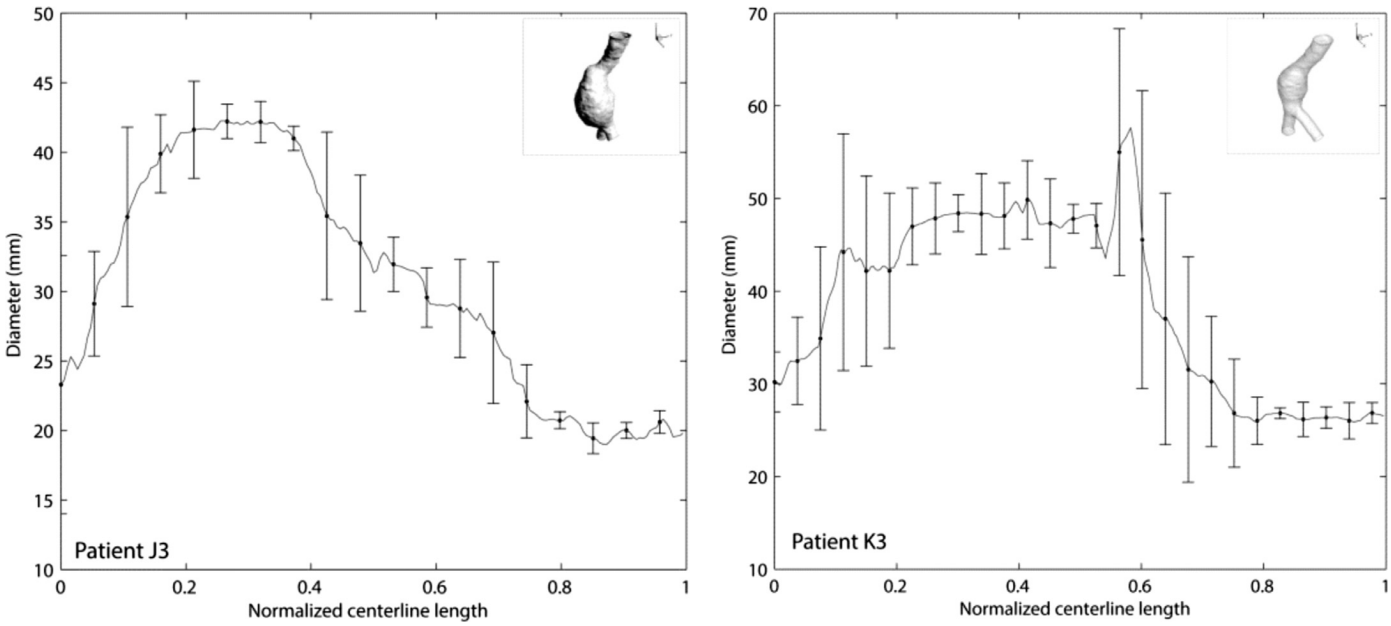

Fig. 7. Uncertainty analysis of orthogonal diameter measurement for two different images from the Patients P08and P9.

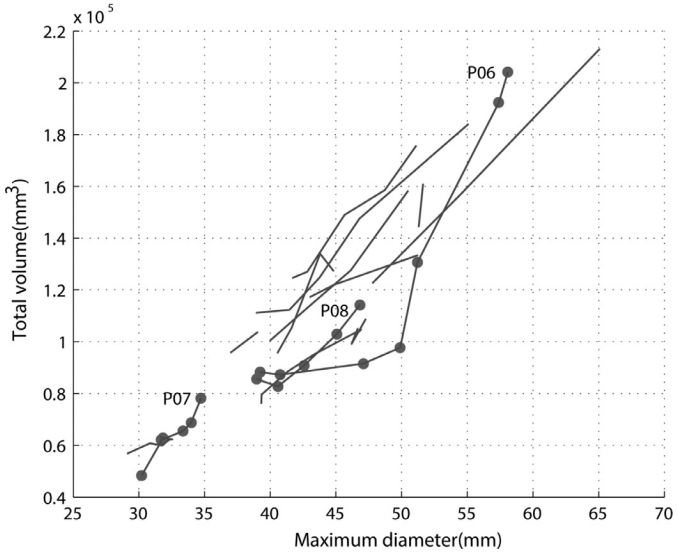

Fig. 8. Expectedly there is a positive correlation between maximum inscribed spherical diameter and total volume of AAAs. To avoid crowdedness, only three of the patients' names are marked on the graph. Each two successive scans are connected with a line on the plot.

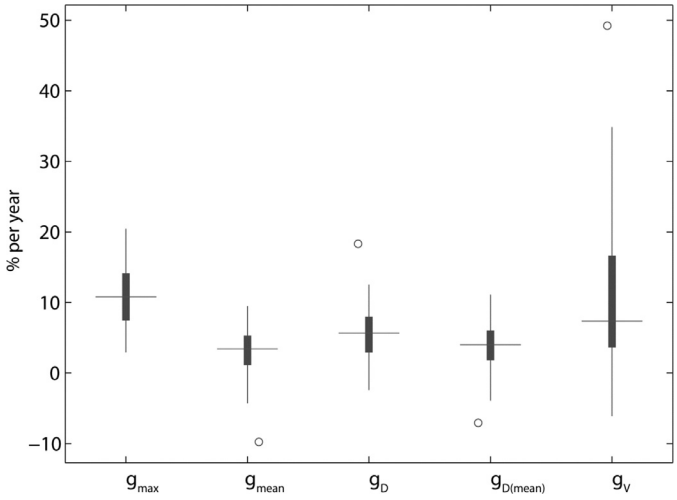

Fig. 9. Box and whisker plots for aneurysm expansions.

Fig. 10 compares growth rate measurements for D, $D(O)$ and $D(A)$. Growth rate measurements of the maximum orthogonal and axial diameter, $g_{D(O)}$ (median 5.08%/year, IQR 6.35%/year) and $g_{D(A)}$ (median 4.99%/year, IQR 5.66%/year) are very similar to that of the inscribed-spherical diameter. There are also correlations between g_V and $g_{D(O)}$ ($r = 0.54$, p-value $= 0.001$) and between g_V and $g_{D(A)}$ ($r = 0.60$, p-value < 0.001).

Table 3
Correlations between key growth rate parameters.

Variable		1	2	3	4	5	6	7	8	9
1	g_{max}	1.00								
2	g_{mean}	0.70	1.00							
3	$g_{max(O)}$	0.71	0.31	1.00						
4	$g_{D(mean)}$	0.75	0.99	0.35	1.00					
5	g_D	0.75	0.60	0.41	0.66	1.00				
6	$g_{D(O)}$	0.56	0.35	0.40	0.42	0.77	1.00			
7	$g_{max(A)}$	0.48	0.10	0.61	0.20	0.52	0.48	1.00		
8	$g_{D(A)}$	0.53	0.39	0.22	0.47	0.72	0.76	0.49	1.00	
9	g_V	0.53	0.40	0.28	0.48	0.53	0.54	0.53	0.60	1.00

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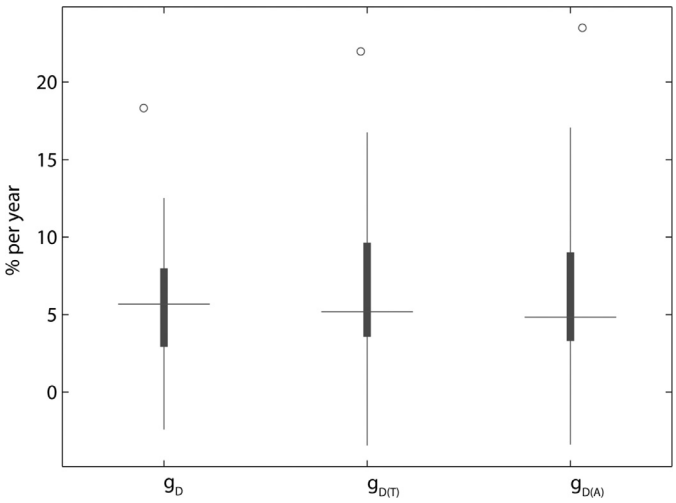

Fig. 10. Growth in maximum diameter for three measurements, inscribed-spherical, orthogonal, and axial diameters.

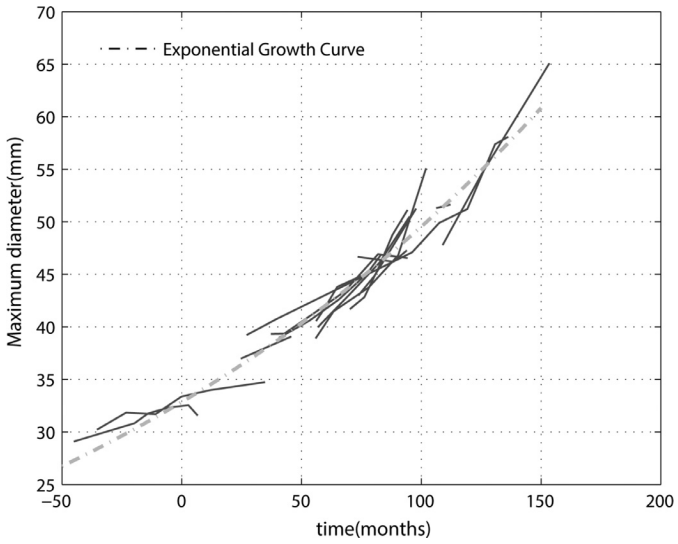

Fig. 12. Exponential growth curve and patients AAA maximum inscribed-spherical diameter growth.

Growth rates in the diameter of the aorta for three measurements are compared in Fig. 11. The averages of growth in the diameter are not different for the three measurement methods. Conversely, the fastest growth of the aorta varies considerably for each of the different measurement methods, $g_{\max(O)}$ (median 15.69%/year, IQR 12.79%/year) and $g_{\max(A)}$ (median 16.88%/year, IQR 12.46%/year). Correlation studies are done between maximal growth of axial, inscribed-spherical, and orthogonal diameter measurements ($g_{\max(A)}$, $g_{\max}$, $g_{\max(O)}$). It is worth mentioning that no correlation was found between $g_{\max(O)}$ and g_V in addition to a weak correlation between $g_{\max(O)}$ and $g_{D(O)}$ (p-value = 0.02).

Finally, an AAA growth evolution curve is generated with an exponential function for the maximal inscribed-spherical diameter by translating the time axis, shown for all the patients' data in Fig. 12. In the plot, Patient P07, who has been in earlier stages of AAA in comparison with other patients, is in the less steep zone of the curve. In other words, the patient's aneurysm is expanding at a lower rate than a patient in a more advanced stage. The slope of the growth has, in general, a trend of increasing with the time, which is consistent with other studies [15,16,21,27,29]. The parameter g found for this curve is 5.06%/year, which is near the median of $g_{D_{\max}}$.

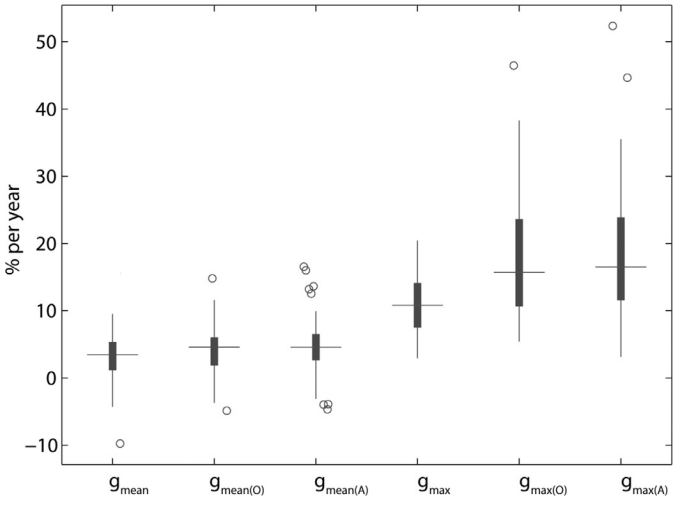

Fig. 11. Mean and maximum growth parameters in diameters for three measurements.

4. Discussion

As suggested in multiple studies, orthogonal diameter is a more realistic way to measure the diameter than the diameter measured on the axial plane [12,13]. This measurement provides more information about the shape of AAAs, in comparison with other methods, which leads to a more accurate AAA diameter for the therapeutic decisions [35]. Finding the diameter on an orthogonal plane, however, is not a definite procedure [3]. Therefore several replacements have been proposed in different studies [12,13,36]. For instance, Dillavou et al. [36] suggested that the diameters of the minor axis on the axial planes is more reproducible than the major axis and has the best correlation with orthogonal diameter, thus, it possibly has more applicability for clinical AAA treatment. The inscribed-spherical diameter, introduced in this paper, is a 3D version of the diameter of the minor axis on the orthogonal plane. Apparently, for all AAAs, the mean and maximum diameter is smaller than those of the axial and orthogonal diameter measurements: mean differences between maximum diameters of inscribed-spherical measurement with two others were 8 and 4 mm, respectively.

Although the idea of using a maximally inscribed sphere for generating the centerline is not novel [31–33], it has not been reported in the AAA's diameter measurement before. This method is, hence, applied to AAAs for enhancing its prediction capability, is evaluated with quantification of several parameters, and is studied for the correlation analysis between the parameters. In this paper, this centerline generation algorithm exploits different AAA diameter measurement methods. The results showed their low sensitivity to different variables, such as steps sizes, choice of the outlet planes, and initial guesses. Besides the centerline using this algorithm generation was completely automated.

The mean values of growth rates in maximum diameters (e.g. g_D, $g_{D(O)}$and $g_{D(A)}$) are not considerably different for the three measurement methods. Nonetheless, the fastest growth of an aorta computed from the inscribed-spherical diameter measurement has the narrowest range among the different measurement methods ($g_{\max}$, $g_{\max(O)}$ and $g_{\max(A)}$ shown in Fig. 11). Both $g_{\max}$ and $g_{\max(A)}$ are highly correlated with growth rate of volume. Particularly, these parameters (fastest growth in the diameter and volume) have been associated with structural wall integrity and stress distribution [16,26]. Meanwhile, $g_{\max(O)}$ does not appear to be correlated with g_V. Besides, only a poor correlation is reported between these two parameters in Martufi

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et al. [16] which reinforces our results. It is worthy to note that the growth rate in the diameter at the exact same position ought to be considered to quantify this parameter which is not practically achievable due to uncertainties in various variables, for example changing posture of the patient during the longitudinal, different scans. In addition, according to what was observed in Fig. 4, some of the shape related attributes of the AAA geometry may reflect in quantification of this parameter. These features' effects may vary by the nature of the different measurement methods.

Finding the plane orthogonal to the centerline could also be a source of inaccuracy in orthogonal diameter measurement. Based on the uncertainty analysis, an error of 5° in determining the orthogonal plane can cause up to 15 mm of miscalculation in measuring the AAA's diameter shown in Fig 7. Finally, in axial and orthogonal diameter measurements, some irregular aneurysmal shapes require an additional manual measurement process, especially if a detailed pointwise quantification of the growth rate of the diameter along the centerline is planned.

Associated with determining surgical interventions and surveillance of interval time, The growth rate calculation using the AAA wall geometry has been proved to be crucial in assessing the risk of rupture [2,12,15,16]. Although a growth pattern captures reasonable AAA growth behavior, shown in Fig. 12, growth rates vary for patients, which is believed to be associated with factors such as advanced age, severe cardiac disease, effect of intraluminal thrombus, and a history of tobacco use [37,38]. Nonetheless, monitoring a growth rate of a single criterion like maximum diameter, which is currently used in clinical practice, may not provide sufficient information [3,16].

Correlation analysis displays that the growth rate of volume is correlated with the growth rate of maximum diameter using each one of the methods. This relationship shows that monitoring the change of maximum diameter over time could lead to finding the growth in volume in cases where the volume's growth is chosen as the major criteria for decision making for a therapeutic procedure. As mentioned before, the growth rate of the volume is correlated with the fastest growth of an aneurysm (g_{max}). Additionally, the fastest growth of an aneurysm was found to be fairly correlated with the growth rate of maximum and average diameter. In other words, by finding an expansion rate of the maximum diameter of an AAA, which is more applicable in clinical practice, and an average diameter over the centerline, a prediction of the fastest growth in diameter can be made.

The maximally inscribed-sphere method, by its nature, reduces the roughness of the surface of the geometry. As a result of this feature, there are, however, possible shortcomings in terms of the diameter measurement. First, the inscribed-sphere diameter measurement produces lower values as a measure for the size of an AAA. This, in fact, is not very desirable if this diameter measurement is used as a single criterion in clinical practice. Second, this diameter measurement may not be able to capture local expansions on the aneurysm surface. Due to these shortcomings, the maximally inscribed sphere method generates the centerline and the orthogonal diameter measurement is used as a key criterion for the rupture potential, while the inscribed-spherical diameter measurement may be used as a complementary aid for predicting AAA growth rate. Regardless of these limitations, this method seems to provide valuable information about size related expansion of aneurysms and produces acceptable growth rate parameters with meaningful correlations.

5. Conclusion

All the measurements used in this study, albeit to different extents, are reliant on the same centerline. Establishment of the centerline, executed completely automatic, showed very low variability to different parameters for instance step size, initial guess and outlet planes.

Using different measurement methods to quantify the diameter of an AAA reflects different values, which may lead to different interpretations from both static and dynamic points of view. While each method has its own unique capabilities and shortcomings, orthogonal measurement seems to remain the gold standard for therapeutic decision making by clinicians. Nevertheless, the inscribed-spherical diameter showed to deliver useful information about the evolution of the size of the abdominal aorta in AAA patients.

The exponential growth curve is the empirical model of the evolution of AAA size, here marked by the diameter over time. Using this pattern, the stage of AAA and the future of the AAA expansion can be speculated for each patient. Therefore, future monitoring and treatment procedures can be planned to minimize treatment risks in AAA patients.

Conflict of interest

The contents of solely the responsibility of the authors and does not necessarily represent the official views of the NIH and NSF. We wish to confirm that there are no known conflicts of interest associated with this publication.

We declare that we have no significant competing financial, professional or personal interests that might have influenced the performance or presentation of the work described in this manuscript.

We confirm that the manuscript has been read and approved by all named authors and that there are no other persons who satisfied the criteria for authorship but are not listed. We further confirm that the order of authors listed in the manuscript has been approved by all of us.

We confirm that we have given due consideration to the protection of intellectual property associated with this work and that there are no impediments to publication, including the timing of publication, with respect to intellectual property. In so doing we confirm that we have followed the regulations of our institutions concerning intellectual property.

Ethical approval

We further confirm that any aspect of the work covered in this manuscript that has involved human patients has been conducted with the ethical approval of Internal Review Board approvals at Michigan State University and Seoul National University Hospital.

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