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Research Article

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Preclinical Validation of Automatic Mitral Valve Segmentation and Measurement Technology for Planning Transcatheter Edge-to-edge Valve Repair Using Computed Tomography

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Abstract

Background: Mitral regurgitation (MR) is one of the most common valvular heart diseases, though many patients with severe MR are unsuitable for surgical interventions. Transcatheter edge-to-edge repair (TEER) is an established non-surgical procedure that allows safe and effective reduction of MR in high-risk patients. Appropriate patient selection is critical and achieved through clinical assessment and imaging derived measurement of the mitral valve (MV) apparatus to optimize procedural success.

Objective: We have developed a technology to automatically measure the MV structure based on computed tomography (CT) imaging data. The primary objective of this study is to compare automatically derived measurements to manually derived measurements performed by expert readers, in patients with MV disease.

Methods: The MV and left-sided cardiac chambers were assessed by 4D CT in 28 patients with MV disease of varying type and severity. MV measurements (MVM) were performed with a fully automatic MV shape extraction algorithm, which provides a means to automatically measure the annulus area, annulus perimeter, anteroposterior (AP) diameters, the inter-commissural (IC) diameters, D-shaped perimeter, and aorto-mitral (AM) angle. These automatically derived measurements were compared to manual measurements performed by experienced cardiologist designated as expert readers.

Results: Our results suggest that for annulus area, annulus circumference, D-shaped annulus circumference, and intercommissural diameter measurements there is a strong correlation between MVM and expert readers (all correlation coefficients(CC), $r > 0.8$). There was slightly less observer (Obs) variability between MVM and the expert readers than between individual expert readers.

Conclusion: The measurement of structural dimensions of the MV using this novel technology demonstrates a significant and strong correlation to manually derived measurements performed by expert readers, and its variability is consistent with inter-Obs variability. We found that key structures of the MV could be measured within 10 seconds and with a 100% success rate. We limited the number of structures measured for this evaluation; however, it is possible to perform several additional measurements that are currently being evaluated. We believe that a streamlined workflow with a more efficient resource utilization can be achieved using this automatic, accurate, and non-Obs dependent technology.

Keywords

Procedural planning, Mitral valve, Automated measurement, Computed tomography

Introduction

MR is one of the most common forms of valvular heart disease, and in addition to surgical intervention there are several new transcatheter procedures available. Adequate patient selection through clinical assessment and imaging modalities remains a key factor for procedural success [1]. Echocardiography is commonly used to assess various inclusion and exclusion criteria for selection of candidates that will benefit from TEER of the MV. While echocardiography provides important information on the morphology and function of the valve leaflets, CT is also being used for pre-procedural workup based on its ability to provide images with a high degree of spatial resolution that could improve accuracy of measurements and enhance understanding of the morphology and function of the valve [2]. There are currently software applications available that offer semi-automated measurement of the MV but require manual intervention which has the potential to introduce measurement error and inconsistent results.

We have developed and are refining an application to automatically perform key measurements on the MV apparatus using CT imaging data, and the goal of this study is to provide a preclinical validation of the application. In addition to providing an alternative to the current manual measurements, this automated approach could eventually be incorporated into a broader framework for procedural planning of TEER and predicting outcomes related to variables such as device type, size, positioning, or number of devices used.

Methods

Data collection

Electrocardiogram (ECG) gated 4D-CT imaging data from 28 patients with MR were retrospectively collected at the Copenhagen University Hospital under institutional guidelines, anonymized and de-identified prior to use in this study. The study cohort included 15 males, median age 64 years, all with severe MR. The inclusion criteria for this study were that the patient had severe MR and had a previous CT study that conformed to technical requirements.

The CT scans were done as part of pre-procedural planning in elective patients for minimally invasive MV surgery. The scan protocol was as follows: the cardiac CT scan protocol included contrast-enhanced, ECG gated CT angiography. Oral beta-blockers were administered to patients with a heart rate exceeding 60 bpm.

Image acquisition was conducted using a 640-slice multiple detector CT system (Aquilion ONE, Vision Edition, Canon Medical Systems, Otawara, Japan) with a gantry rotation time of 275 ms and detector collimation of 0.5 × 320. Tube voltage was adjusted between 100 and 120 kV, while tube current varied from 280 - 500 mA based on participants' body mass index.

Intravenous contrast media (Visipaque, 60 - 80 ml, 320 mg/ml) was administered at a flow rate of 6 ml/s, followed by a saline chaser. Cardiac CT was triggered automatically using a region of interest in the descending aorta with a threshold of 250 Hounsfield units.

The ECG gated cardiac CT sequences included 20 volumes per cardiac cycle in 5% increments, where each volume contains 53 - 240 slices with 512 × 512 pixels. The in-slice resolution is isotropic with 0.429 - 0.431 mm and slice thickness of 0.50 - 2.00 mm. Data was acquired at the 75% cardiac phase (diastolic phase) in the R-R interval to be used for analysis in both the automatic and manual measurements.

The MVM application was implemented, and studies managed, on a Vitrea workstation (Canon Medical Systems Corporation, Otawara, Tochigi, Japan)

Automatic segmentation and measurement

Our deep learning-based MV segmentation method (MVS) [3] is used for the analyses. The MVS outputs quadmesh coordinates consisting of 19 × 9 points for the anterior leaflet and 25 × 9 points for the posterior leaflet using the following six steps: (1) CT images are obtained from the functional cardiac CT examination, (2) The MV region is roughly detected from the CT image input based on left atrial and left ventricular region, (3) The CT Image is cropped to focus around the MV region, (4) Probability map inference method is calculated using 3D U-Net [4] to distinguish the anterior leaflet, posterior leaflet and background, (5) Shape extraction of the MV is performed based on DenseNet-121 [5] with the probability map and outputs 3D quadmesh coordinates for the anterior and posterior mitral leaflet, (6) The final MV mesh is generated. It should be further noted that this pre-clinical validation study did not use the CT images used in the development of MVS. We believe that the unique attribute of our method is that it improves segmentation accuracy by using probability maps.

MVM is a method of automatically calculating measurements related to MV morphology based on the mesh calculated by MVS. Six measurements are calculated as follows; (1) Annulus area, (2) Perimeter are calculated from the closed curve connecting the outermost grid points (x = 0), (3) D-shaped annulus perimeter from the closed curve for annulus and positions on its closed curve closest to the trigones whose point is calculated by MVS; (4) IC diameter is the distance between anterior commissure point (x = 8, y = 0) and posterior commissure point (x = 8, y = 18) on the anterior leaflet mesh, (5) AP diameter is the distance between the midpoint of the open curve connecting the outermost grid points (x = 0) of the anterior leaflet mesh and the midpoint of the open curve connecting the outermost grid points of the posterior leaflet mesh, and (6) AM angle is calculated from the MV axis calculation based on the MV mesh by MVS and the aortic valve axis calculated based on the aortic root by the method described by Aoyama et al. [6]. Anterior and posterior leaflet lengths, which are important for planning of MV interventional treatment, were excluded from this study because the interventionalist typically uses both imaging and non-imaging data for determining the clip placement, and such cross sections cannot be automatically identified.

Semi-automated measurement

Three experienced cardiologists participated in this validation study as expert readers and were blinded to the re-

sults of the automated measurement algorithm. CT cases were opened using the 3 mensio structural heart (version 10.3, Pie Medical Imaging B.V., Netherlands) viewer, and the expert readers performed semi-automated measurement of the parameters mentioned above using this application which complies to the standard procedure adopted by our lab. The reading physicians had been trained on a standardized measurement protocol using this application, and measurement data was saved in an MV report.

Statistical analysis

Continuous data was given as mean and standard deviation (±SD) for cases. For each measurement, the inter-Obs differences between automatic and manual measurements were also presented as mean and standard error (SE). Those relations were analyzed by Pearson's product–moment CC (r), scatterplot and the Bland–Altman difference plot with 1.96 SD intervals. The fixed errors between them were analyzed by the paired-t test, and the proportional errors were analyzed by Pearson's product–moment CC (r_p) between the difference and the mean between them. IBMSPSS Statistics (version 26.0, IBM, New York, NY, USA) was used for all statistical analysis. In this study, Bonferroni correction was used to adjust for multiple validation endpoint in the 6 measurement items, and significant differences were considered if $p < 0.0083$.

Results

Automatic measurements were successfully processed for all 28 cases yielding a 100% success rate. 22 patients had sinus rhythm during CT scan whereas 6 had atrial fibrillation. However, this did not hamper the image quality and semi-automated and automated segmentation could be performed.

MV morphology can change depending on the cardiac phase and MR grade; however, our algorithm was able to generally segment all valves in each condition. On the other hand, 3 mensio structural heart software could not be analyzed for one case due to truncated LV yielding a 96% success rate.

Table 1 shows the measurement results and table 2 shows inter-Obs results. For annulus area, annulus circumference, D-shaped annulus circumference, intercomissural diameter (AL-PM diameter) and AP diameter, there was a significant and strong correlation ($r > 0.8$) between MVM and the expert readers. The strength of correlation between manual measurements by physicians and automatic measurements by MVM is comparable to the strength of correlation between physicians. For AM-angle, correlations are weaker not only among physicians and MVM, but also between physicians more than is observed for other measurements. Correlation between Obs1 and Obs2 is strong ($r = 0.89$), while correlation between Obs1 and Obs3 and between Obs2 and Obs3 is weak ($r = 0.38$). Correlations between MVM and each Obs are moderate (0.41 - 0.56). A fixed error was observed in most comparisons. MVM tends to be slightly larger than the manual measurements generated by the expert readers in all measurements except the AM angle. There was no significant proportional error observed except for Obs3-MVS for annuus area and AM angle.

Computational processing time is observed using equipment as shown in table 3. For each single image data, it is seven seconds without including loading and writing time. If there are 20 phase image data, total processing data for one patient will be 140 seconds (Figure 1, figure 2, figure 3 and figure 4).

Discussion

The primary objective of this study was to determine how automated measurements generated by the MVM application compared to manual measurements made by expert physician readers. Accuracy validation results show a strong correlation ($r > 0.8$) between automated processing and manual processing. This suggests that automatic processing can be substituted for manual processing by a skilled reader, though we have noted automatic measurements tend to be slightly larger than the manual measurements. We believe this could be due to the automatic measurements being made in a 3-dimensional model whilst the application (3 mensio) used for manual measurements operates in a 2-dimensional plane, and that 3D measurements more accurately represent MV morphology. However, it has not been verified whether 3D or 2D measurements are superior in actual treatment planning. This is a subject for future research. And when using computerized automatic measurement algorithms, not limited to MVM, users need to understand and consider the specific properties of the automatic measurement algorithms being implemented. There is also a slight difference in AM angle calculations. We postulate that this could be related to the method of identifying the plane used for calculating the AM angle, which is not well defined. We are currently investigating ways to improve the AM angle measurement algorithm with reference to the manual measurement position of the physician.

The processing time of 7 s per phase for MVM was significantly faster than manual measurement by expert readers. We propose that with this rapid processing time and a pro-

Table 1: Mean values among cases for each six measurements by Obs1, Obs2, Obs3, and MVS, respectively.

	Obs1	Obs2	Obs3	MVS
Annulus area (mm^2)	1556.67 ± 447.61	1710.00 ± 431.44	1492.963 ± 420.68	1952.574 ± 511.4864
Annulus perimeter (mm)	144.93 ± 20.79	160.83 ± 19.14	147.03 ± 18.92	160.88 ± 20.81
D-shaped perimeter (mm)	102.20 ± 17.07	114.50 ± 17.07	108.77 ± 16.24	153.74 ± 19.16
IC diameter (mm)	46.90 ± 7.37	47.19 ± 5.95	44.56 ± 6.27	52.22 ± 6.79
AP diameter (mm)	39.70 ± 5.70	46.26 ± 6.78	41.59 ± 6.11	45.47 ± 7.37
AM angle (degree)	48.36 ± 7.91	53.70 ± 6.39	57.59 ± 10.16	44.60 ± 5.66

Table 2: Presents the inter-Obs differences, CC, the fixed errors, and the proportional errors between automatic and each manual measurement.

	Obs1 - Obs2	Obs1 - Obs3	Obs2 - Obs3	Obs1 - MVS	Obs2 - MVS	Obsr3 - MVS
Annulus area difference (SE)	-153.33 (37.99)	63.70 (29.17)	217.03 (27.48)	-395.91 (54.58)	-242.57 (38.63)	-459.61 (35.53)
CC, r	0.90*	0.94*	0.94*	0.83*	0.92*	0.94*
Fixed error, p	< 0.001*	0.038	< 0.001*	< 0.001*	< 0.001*	< 0.001*
Proportional error, rp	0.084	0.18	0.076	-0.24	-0.41	-0.50*
Annulus perimeter difference (SE)	-15.90 (2.32)	-2.10 (1.46)	13.80 (1.85)	-15.95 (2.40)	-0.05 (1.91)	-13.85 (1.68)
CC, r	0.82*	0.93*	0.87*	0.82*	0.88*	0.91*
Fixed error, p	< 0.001*	0.16	< 0.001*	< 0.001*	0.98	< 0.001*
Proportional error, rp	0.14	0.25	0.023	-0.0013	-0.17	-0.22
D-shaped perimeter difference (SE)	-12.30 (1.96)	-3.06 (3.31)	9.24 (4.04)	-51.55 (2.13)	-39.25 (1.87)	-48.49 (4.09)
CC, r	0.82*	0.91*	0.83*	0.82*	0.86*	0.92*
Fixed error, p	< 0.001*	< 0.001*	0.0048*	< 0.001*	< 0.001*	< 0.001*
Proportional error, rp	-0.001	0.12	0.09	-0.2	-0.22	-0.4
IC diameter difference (SE)	-0.29 (0.56)	2.33 (0.49)	2.62 (0.47)	-5.32 (0.84)	-5.03 (0.74)	-7.66 (0.70)
CC, r	0.93*	0.94*	0.92*	0.81*	0.83*	0.85*
Fixed error, p	0.612	< 0.001*	< 0.001*	< 0.001*	< 0.001*	< 0.001*
Proportional error, rp	0.5	0.44	-0.14	0.14	-0.23	-0.15
AP diameter difference (SE)	-6.56 (0.72)	-1.89 (0.60)	4.67 (0.58)	-5.78 (1.04)	0.79 (0.59)	-3.89 (0.80)
CC, r	0.84*	0.87*	0.90*	0.69*	0.91*	0.83*
Fixed error, p	< 0.001*	0.0038*	< 0.001*	< 0.001*	0.2	< 0.001*
Proportional error, rp	-0.3	-0.14	0.23	-0.34	-0.2	-0.32
AM angle difference (SE)	-5.34 (0.71)	-9.23 (1.97)	-3.89 (1.87)	3.76 (1.34)	9.10 (1.09)	12.99 (1.80)
CC, r	0.89*	0.38	0.38	0.52*	0.56*	0.41
Fixed error, p	< 0.001*	< 0.001*	0.047	0.0094	< 0.001*	< 0.001*
Proportional error, rp	0.42	-0.26	-0.46	0.37	0.15	0.56*

Note: *Showed p < 0.0083.

Table 3: List of the equipment used for implementing the automated MV measurement software.

OS	Microsoft Windows 10 Enterprise
System type	64-bit Operating System
Processor	Intel(R) Core(TM) i7-9800X CPU @ 3.80GHz 3.79 GHz
Processor number	16
GPU CARD	NVIDIA GeForce RTX 3090(24GB) (only for leaning phsae)
RAM	128 GB

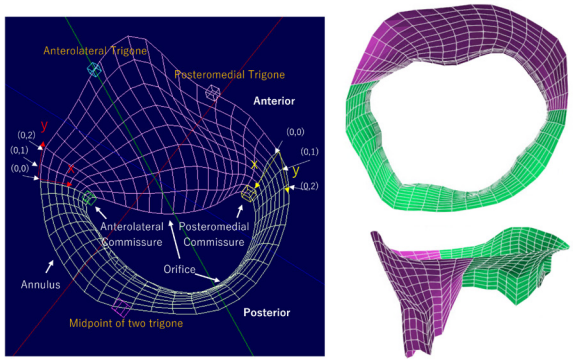

Figure 1: The MVS generated MV mesh is illustrated.

cessing success rate of 100%, MVM could be efficiently incorporated into a routine clinical workflow. When we consider future product implementation, this high processing success rate could enable background processing without an operator. This could dramatically improve medical staff efficiency and resource allocation.

We believe that the potential impact of automatic visualization and the measurement of MV morphology and motion on treatment planning is two-fold. First, there is an opportunity for labor savings in that an imaging technologist could run an application to measure the MN, freeing the cardiologist or radiologist from performing the manual task. Secondly, if ongoing clinical studies demonstrate that MVM is a more consistent non-Obs dependent measurement of the MV, there is a potential to improve the quality of information available for TEER procedural planning.

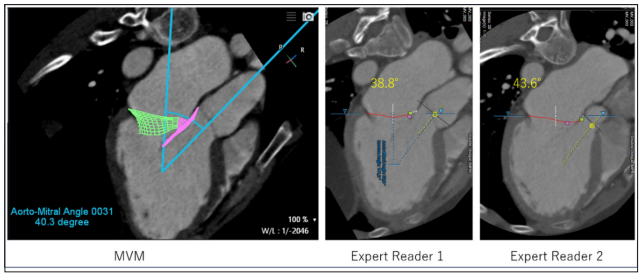

Figure 2: Comparison of measurement location by MVM and readers for AM angle.

Figure 3: The automated MVM application and results. The system can perform several measurements in addition to those included in this study.

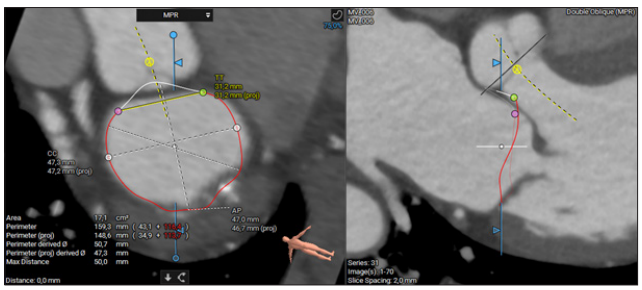

Figure 4: Manual measurements from the CT studies were performed using the Pie medical 3mensio structural heart application, routinely used by the interventional team.

Limitations

This evaluation was based on a relatively small study population, which may not accurately reflect the feasibility of automated measurements in certain subsets of patients. The anterior and posterior leaflet lengths, which are important for planning of MV interventional treatment, were excluded from this study because physicians need to determine the 2D cross section where these measurements should be measured using information other than images.

LV systolic and diastolic phases are variably defined in different studies. In this study, we decided to define the reference phases based on the LV and LA volume curves. CT has limited temporal resolution which makes it difficult to define the exact continuous velocity and dynamics in between the available captured phases of the cardiac cycle R-R interval.

Conclusion

In this paper we have presented a new application designed to automatically measure the MV structure within 10 seconds and with 100% success rate. This preclinical validation study has demonstrated that the MVM algorithm is capable of automatically generating measurements of the MV structure with an accuracy comparable to those performed manually by expert readers. Its variability is more consistent with a significant reduction in inter-Obs variability. We believe that a streamlined workflow and efficient resource utilization can be achieved by this automatic, accurate, and non-Obs dependent technology.

Acknowledgements

None.

Conflicts of Interest

G. Aoyama, K. Kawashima and T. Sakaguchi are Canon Medical Systems Corporation employees. J. Chapman is Canon Medical Informatics employees. K. Kofoed and M. Pham have received research grants for this collaboration from Canon Medical Systems Corporation.

Funding

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Institutional Review Board Statement

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Research Ethics Committee at Juntendo University Hospital on 28 December 2022 (approval number: E22-0388).

Informed Consent Statement

Acquisition of written informed consent was waived by the institutional review board as patient data were retrospectively collected, anonymized and de-identified prior to use in this study.

Data Availability Statement

The data presented in this study is not publicly available due to restrictions imposed by research ethics.

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