balt3/imi-imi/imi-imi/imi00110/imi2225-10z | xppws | S=1 | 1/5/10 | 9:12 | Art: IMI200191 | Input-sv

AQ: 1

Percutaneous Aortic Valve Replacement

Emerging Tractability for Sufficient Intracardiac Resection of the Aortic Valve

René Bombien, MD, Claudia Lesche,† Lucian Lozonschi, MD,‡ Max Feucker,* Ralf Brinkmann, PhD,§ Christian Dahmen, MSc,¶ Michael Schünke,‖ Jochen Cremer, MD,* and Georg Lutter, MD, PhD**

AQ: 2

Objective: The feasibility of endovascular resection of highly calcified aortic valves has already been demonstrated by our group. Different endovascular and intracardiac tractability methods were applied. In this study, these technologies were analyzed comparing the tractability, the resection time, and the lesions in the surrounding tissue.

Methods: All aortic valve resections (seven human hearts and 21 porcine hearts) were performed using a Thulium:YAG laser (continuous wave, wavelength of 2.01 μm, 20 watts power rating). In the first resection system, the laser fiber was controlled by a free in-lying flexible endoscope (Ø 2.5 mm, length of 600 mm). The distal part of the endoscope (40 mm) was moved in one plane by proximal manual
AQ: 3 control (three degrees of freedom). Second, the resection system was
AQ: 4 separated into defined rooms assigning one room for one tool. The fiber was controlled by the above-mentioned endoscope (*) (three degrees of freedom). The third resection system was a mechanical microactuator carrying the laser fiber (three degrees of freedom). The fourth resection system contains a rotatable inlay with defined rooms and a newly designed nitinol (NiTi) microactuator that controlled the laser fiber (four degrees of freedom). The resection time per leaflet was measured in minutes. Gross anatomy and histology in the surrounding tissue were evaluated.

Results: The resection time in approaches 1, 2, 3, and 4 was 5.5 ± 2.3 minutes, 7.4 ± 2.7 minutes, ± 6.6 minutes, and2.3 ± 1.2 minutes, respectively. The gross anatomy and histology of collateral damages revealed only superficial lesions of the surrounding tissue. The amount of lesions and the resection time were lower in the fourth approach with four degrees of freedom.

Conclusion: This analysis demonstrated that a precise tractability with four degrees of freedom is necessary for a faster and safer endovascular resection of the aortic valve. The analysis will help to optimize the ongoing development of the endovascular and intracardiac resection technology.

Key Words: Resection, Microactuator, Human, Aortic valve, In situ.

(*Innovations* 2010;5:000–000)

Accepted for publication November 1, 2009.

From the *Department of Cardiovascular Surgery, University Hospital Schleswig-Holstein, Campus Kiel, Kiel, Germany; †Institute of Microtechnology, University of Braunschweig, Braunschweig, Germany; ‡Division of Cardiothoracic Surgery, University of Wisconsin, Madison, WI, USA; §Institute for Biomedical Optics, University of Lübeck, Lübeck, Germany; ¶Division Microrobotics and Control Engineering, University of Oldenburg, Oldenburg, Germany; and ‖Institute of Anatomy, Christian-Albrechts-University of Kiel, Kiel, Germany.

Presented at the Annual Scientific Meeting of the International Society for Minimally Invasive Cardiothoracic Surgery, San Francisco, CA USA, June 3-6, 2009.

Address correspondence and reprint requests to René Bombien, MD, Department of Cardiovascular Surgery, University Hospital Schleswig-Holstein, Campus Kiel, Arnold-Heller-Strasse 7, D-24105 Kiel, Germany. E-mail: rbombien@quabo.de

ISSN: 1556-9845/10/0501-0001

The current clinical application of catheter-based technologies, especially for transcatheter heart valve implantations, is permanently emerging. A safe guidance and a reproducible accuracy of application are main aspects for intracardiac procedures. Up to now, nearly all valve implantations are designed as single-shot scenes.[1] Only a few experimental publications report on mechanisms to replace a malpositioned valve.[2] However, in the future, it will be essential to offer this technology for a tapering patient collective.

The repositionable valved stent will be one important part. However, to come closer to the golden surgical standard of replacing aortic valves, the severely calcified aortic valve has to be resected before a new valved stent can be implanted.[3,4] Several in vitro, in situ, and in vivo studies demonstrated that an endovascular resection of aortic valves is necessary and will be possible. However, these studies were all of experimental manner.[5–10]

One main goal of the past 6 years development of the resection technology was the emerging tractability of the resection tools. In this study, the development of these endovascular resection tools with mechanical, microactuator-based, and shape memory alloys was evaluated.

MATERIALS AND METHODS

Ethical Fundament for the Experimental Work

Human Preparations

Seven human preparations were obtained from the Institute of Anatomy of the Christian-Albrechts-University of

<zjs;ISMICS Article> • <zjss;ISMICS Article> • <zdoi;10.1097/IMI.0b013e3181ceed96>

Kiel (72 ± 12 years; 69 ± 9 kg; 170 ± 8 cm). This study was conducted in agreement with the basic principles of ethics [Basic Constitutional Law of the Federal Republic of Germany (§1) and Ethic Committee Decision from November 24, 2004 (D 434/04)].

Animals

Animals received humane care as approved by the Centre for Experimental Animal Research at Kiel University [V312–72241.121–6(63–5/06) July 2, 2006] and in compliance with the "Guide for the Care and Use of Laboratory Animals" prepared by the Institute of Laboratory Animal Resources, National Research Council, and published by the National Academy Press, revised 1996.

Resection Methodology

Resection Device and Setup

All sclerotic aortic valves in this study were resected by a continuous wave Thulium:YAG laser system with 20 watts power rating (Tm:YAG: 2.01 μm, ITL Lasergerät SN: #00272001, 380/400V 16 A; LISA laser OHG, Katlenburg-Lindau, Germany). The visualization was realized using an
AQ: 5 additional endoscope with a fiber optic to a digital camera. The resection process was exclusively video controlled (using a 30 in television) and digitally recorded.

Endoscopically Guided Resection

The laser fiber (Ø 365 μm; CeramOptec GmbH, Bonn, Germany) was controlled by a flexible endoscope (Richard Wolf GmbH, Knittlingen, Germany) with an outer diameter of 2.5 mm and a length of 600 mm. The distal part of the endoscope (40 mm) was moved by proximal manual control: flexible in one plane for an angle of 130°/120°, 120° rotatable, and movable forward and backward.

In group A, the resections were performed in seven human preparations from a retrograde approach using one endoscope guiding the laser fiber. The additional instrument, the forceps catheter (Ø 1.3 mm, Richard Wolf GmbH, Knittlingen, Germany), was able to open and close without
F1 target-oriented guidance (Fig. 1). The heart valve was isolated using an aortic valve isolation chamber (AVIC) deployed in a retrograde fashion.[6]

In group B, the resections were performed in seven cadaver porcine hearts and differ from group A in an endoscopically guided forceps catheter. Here, both endoscopes (with a diameter of 2.5 mm and a length of 600 mm; Richard Wolf GmbH, Knittlingen, Germany) were positioned into the AVIC main catheter and each endoscope in its own chain
F2 guide (Fig. 2). The heart valve was isolated with an AVIC deployed in a retrograde fashion.[7]

Microactuator Guided Resection

In group C, the resections were performed in seven cadaver porcine hearts in a transapical antegrade fashion. The applied microactuator was based on a deflectable, mechanical principle.[11] The mechanical actuation concept consists of two sledges that are connected with swivel joints. One sledge is mounted on a catheter (mounting sledge), and the second one carries the surgical resection instrument (carrier sledge). By moving the laser fiber forward and backward, this carrier sledge can be deflected in radial direction by means of the two integrated swivel joints. The variable deflection state gives the possibility to realize a cutting on various radii. Here, three degrees of freedom were realized (Fig. 3). The heart F3
valve was isolated using a transapical AVIC.[7]

In group D, the resections were performed transapically in seven cardiopleged porcine hearts under standard extracorporeal circulation using a pseudoelastic actuator system (Fig. 4). This F4

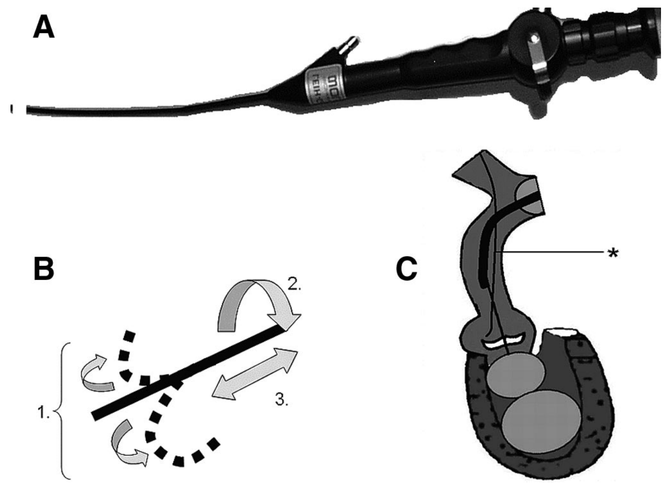

FIGURE 1. A, The laser fiber was controlled by the endoscope. B, The three degrees of freedom were demonstrated in the scheme. C, The endoscopically guided laser fiber (*) was inserted through the right carotid artery to resect the aortic valve. The aortic valve was isolated by two subvalvular balloons and one balloon in the aortic arch.

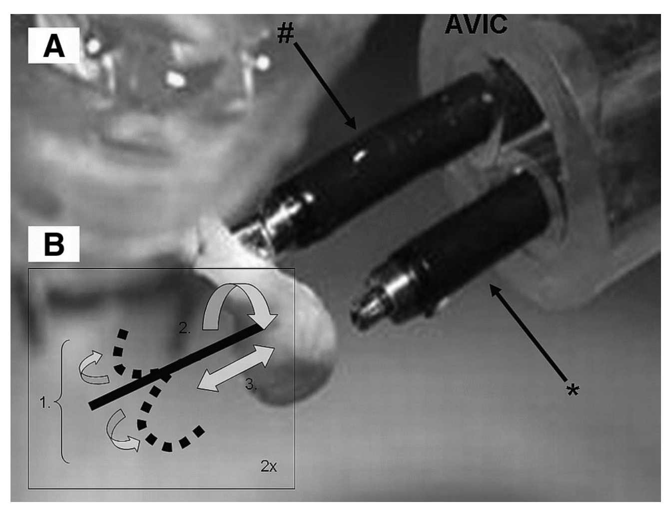

FIGURE 2. A, The AVIC with two separate chain guides and in each chain guide one endoscope. The resected native porcine leaflet is gripped by the endoscopically guided forceps catheter. B, The three degrees of freedom were demonstrated in the scheme. The deflection principle is the same as in group A, and additionally, the forceps catheter is guided.

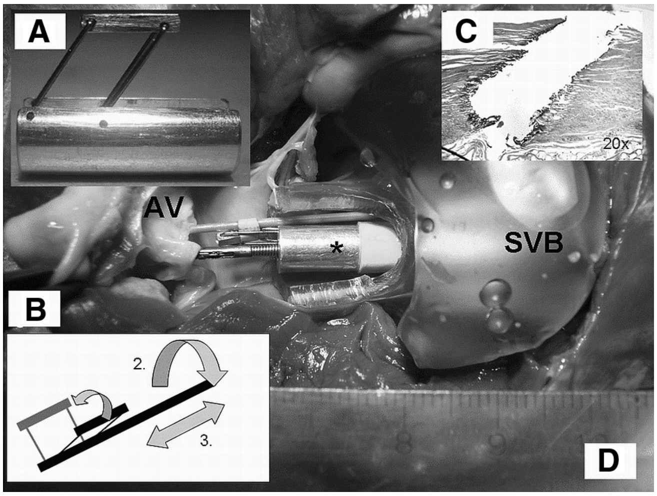

FIGURE 3. A, The mechanical microactuator consists of two sledges that are connected with swivel joints. One sledge is mounted on a catheter (mounting sledge), and the second one carries the surgical resection instrument (carrier sledge). B, The three degrees of freedom were demonstrated in the scheme. C, One complete perforation of the aortic annulus is displayed (HE staining, ×20). D, Experimental setup in a porcine heart. The AVIC was transapically inserted. The subvalvular balloon (SVB) sealed the ventricular side of the resection chamber. One leaflet of the aortic valve (AV) is gripped by the forceps catheter. The microactuator carried the laser fiber (*).

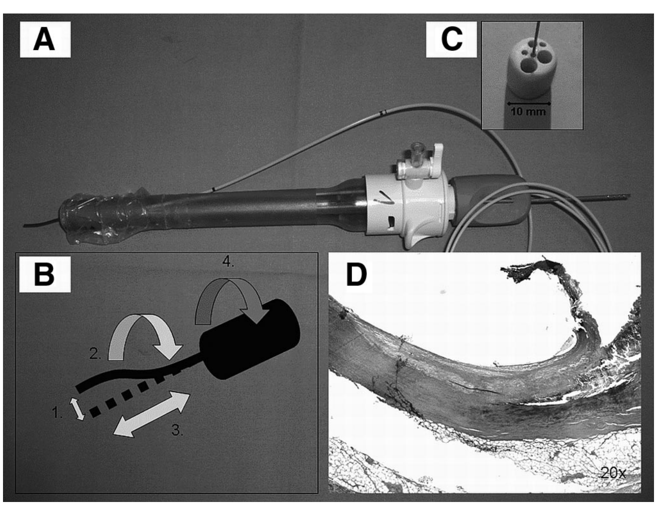

FIGURE 4. A, The AVIC system with the rotatable inlay was inserted transapically into cardiopleged porcine hearts. B, The four degrees of freedom were demonstrated in the scheme. C, The inlay demonstrated the different arrangement of the working channels for the laser fiber, the optic, the forceps catheter, and the irrigation and suction lines. D, The observed superficial lesion of the aortic annulus is shown (HE staining, ×20).

actuation mechanism is based on the pseudoelastic effect of shape memory alloys (SMA). This effect—also known as superelasticity—is due to a crystal modification within the material. Thereby face-centered cubic austenite is restructured to monoclinic martensite by a strong external strain. After reaching a critical stress, the material can be further deformed easily under constant strain. As soon as the strain is stopped, the deformation of the material becomes fully reversible. The actuator system is made of a NiTi SE 508 tube (Euroflex GmbH) with an outer diameter of 1.2 mm and a wall thickness of 0.15 mm. To achieve the desirable S-shape in a straight tube, it is necessary to emboss the shape in a thermal process at 500°C. The device was embedded into the newly designed rotatable inlay of the AVIC. The aortic valve was isolated using a transapical AVIC.[7]

TABLE 1. Resection Times With Different Microsystemic Tools

	Group A	Group B	Group C	Group D
Resection time (min)	5.5 ± 2.3	7.4 ± 2.7	19 ± 6.6	2.3 ± 1.2

Resection times of all groups were displayed as mean ± standard deviation.

Parameters

The resection time was recorded. The data were compared using the Wilcoxon-Mann-Whitney *U* test and the *t* test and were displayed as a box plot. A *P* value <0.05 was considered significant. The statistics were performed using SPSS (version 8.0; SPSS Inc., Chicago, IL). Gross anatomy and histology of the surrounding tissue were evaluated.

RESULTS

Resection

The results of the resection are shown in Table 1. The statistical comparison of the data is expressed in a box plot (Fig. 5). T1 F5

Group A

The resection time was 5.5 ± 2.3 minutes. The endoscopic guidance of the laser fiber was acceptable but not reproducible. Before a laser cut could be performed, several pre–try-outs were necessary to ensure an exact resection line in the annulus. Furthermore, the unsteerable forceps catheter was insufficient for an adjusted gripping of the leaflet. Superficial lesions were found in the aortic annulus and the ascending aorta.

Group B

The resection time was 7.4 ± 2.7 minutes. The endoscopic guidance was affected by the separate chain guides in the AVIC. There was no possibility to gear the resection instruments perpendicular toward one leaflet. Twisting of both endoscopes occurred. The endoscopically guided forceps catheter offers a significantly safer and faster gripping of the leaflet. The gross anatomy and histology observed superficial lesions in the annulus and the ascending aorta.

Group C

The procedure could not be performed with precision. Difficulties occurred mainly in steering the actuator with the laser fiber. A reproducible deflection of the microactuator

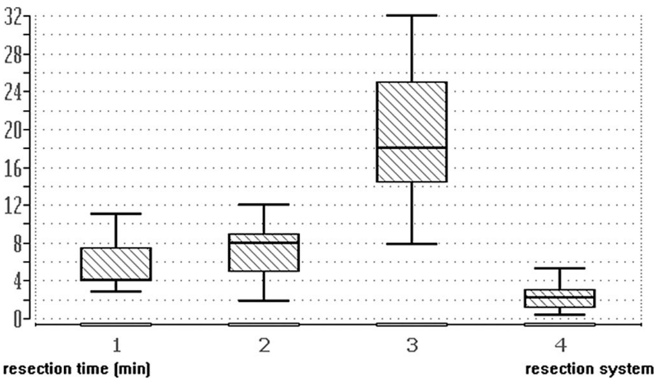

FIGURE 5. The box plot demonstrated significant lower resection times in group D compared with all other groups.

could not be observed. The duration of the resection was 19 ± 6.6 minutes. In three cases, the resection was interrupted. Significant damages of the aortic wall and the aortic annulus were observed (Fig. 3C).

Group D

The combination of the SMA microactuator and the rotatable AVIC inlay offers a good handling and reproducible guidance of the laser fiber. No excessive pre–try-outs were necessary to ensure an accurate resection line. The resection time was 2.3 ± 1.2 minutes. The infinitely variable diameter of the cutting and the perpendicular way to the leaflet offers a safe and fast resection of the leaflets. Only one superficial lesion in the aortic annulus was observed (Fig. 4D).

DISCUSSION

New, innovative transcatheter valve implantation systems are emerging in clinical medicine.[12–14] The current valve implantation procedures from transfemoral or transapical need a totally new operation setup. Combinations of catheter laboratory and cardiac operation room, the so-called hybrid AQ: 6 operation rooms, fusion of preoperative CT data and intraoperative echocardiography data, and the cooperation of anesthetists, interventional cardiologists, and cardiac surgeons were generated in main cardiac health centers.[15]

However, to reduce the field of application to sole implantations of aortic valves in multimorbid patients will not be effective. The offer of this high-end medicine to younger patients will require a perfect replacement technique with a better outcome compared with the golden standard of open heart valve surgery with extracorporeal circulation and with a minimum of risk.[16–18]

Hence, a consecutive resection of the diseased valve will be a milestone on the way to the golden standard. However, to ensure an optimal and safe resection of the valve, the design of optimal instruments is ongoing.

In this study, different stages of development in these microactuator instruments show that a gain of degrees of freedom significantly influences the resection outcome.

In the endoscopes, the Bowden concept, deflection based on cable-rope pull, offers movements in one plane. The second plane was realized by a rotation of the whole endoscope. And the way forward and backward displays the third degree of freedom. The mechanical microactuator uses the same principle. However, the resection procedures show poor results because of the indirect move of the actuator operated by the laser fiber.

By adding an additional rotation to the whole resection unit, the procedure was significantly faster compared with the mechanisms used in groups A, B, and C. Now, the operation process was adjusted to one leaflet. Before the resection procedure was started, the forceps catheter was brought perpendicular to the tip of the leaflet, then the inlay was rotated until both, the SMA and the optic, were perpendicular to the leaflet. The forceps catheter was synchronously rotated to the contra point. Consequently, the leaflet was stretched and offers optimal resection circumstances. On one hand, this rotatable inlay offers the optimal perpendicular position onto the part of the aortic valve that has to be resected; on the other hand, a fourth degree of freedom was implemented.

Particularly, the progress of enhancing resection tools was also demonstrated as a function of fewer lesions in the surrounding tissue. The increased resection accuracy with the SMA inlay tool offers optimal conditions for a tissue-gentle procedure.

To optimize and to accelerate the resection process, a synergy of different visualization methods and the combination to a computer-assisted guidance of the tools will be necessary.[19] A first concept for the system and the needed technologies to be developed has been proposed elsewhere.[20]

Furthermore, the sufficient isolation of the heart valve will be the basis for a safe resection of the valve. An isolation of the pulmonary valve in a beating porcine heart for 5 minutes was recently demonstrated (Bombien et al., manuscript in preparation). Therefore, a method to resect the valve AQ: 7 within 5 minutes will be required. The SMA inlay resection method is promising for a successful use in a beating heart.

CONCLUSIONS

This analysis demonstrated that a precise tractability with four degrees of freedom is necessary for a fast and safe endovascular resection of the aortic valve. This analysis will help to optimize the ongoing development of the endovascular and intracardiac resection technology.

LIMITATIONS AQ: 8

In this study, the four models were different, but the resection process from the positioning of the catheter system to the finished removal of the leaflets was standardized. Therefore, the analyzed parameters were similar in all models, and the results were considered as comparable.

Furthermore, the resected human aortic leaflets were sclerotic not highly calcified. The porcine aortic leaflets were not pathologically diseased. Owing to the experimental appendage, the presented systems are not yet ready to be used in vivo, but the results will pave the way for future enhancement.

ACKNOWLEDGMENTS

Dr. Bombien thanks his PhD students for their contribution to the work. The authors thank Gerburg Lutter and Lasse Bombien.

REFERENCES

1. Vahanian A, Alfieri O, Al-Attar N, et al. Transcatheter valve implantation for patients with aortic stenosis: a position statement from the European association of cardio-thoracic surgery (EACTS) and the European Society of Cardiology (ESC), in collaboration with the European Association of Percutaneous Cardiovascular Interventions (EAPCI). *EuroIntervention.* 2008;4:193–199.
2. Lauten A, Ferrari M, Petri A, et al. Experimental evaluation of the JenaClip transcatheter aortic valve. *Catheter Cardiovasc Interv.* 2009; 74:514–519.
3. Lutter G, Kuklinski D, Berg G, et al. Percutaneous aortic valve replacement: an experimental study. I. Studies on implantation. *J Thorac Cardiovasc Surg.* 2002;123:768–776.
4. Lutter G, Ardehali R, Cremer J, Bonhoeffer P. Percutaneous valve replacement: current state and future prospects. *Ann Thorac Surg.* 2004;78:2199–2206.
5. Quaden R, Attmann T, Boening A, et al. Percutaneous aortic valve replacement: resection before implantation. *Eur J Cardiothorac Surg.* 2005;27:836–840.
6. Quaden R, Attmann T, Schünke M, et al. Percutaneous aortic valve replacement: endovascular resection of human aortic valves in situ. *J Thorac Cardiovasc Surg.* 2008;135:1081–1086.
7. Quaden R, Attmann T, Klaws GR, et al. Percutaneous aortic valve replacement: endovascular sealing studies in situ. *Innovations: Technol Tech Cardiothorac Vasc Surg.* 2008;3:27–32.
8. Bombien RH, Appel M, Attmann T, et al. Percutaneous aortic valve replacement: gross anatomy and histological findings after transapical and endoluminal resection of human aortic valves in situ. *Eur J Cardiothorac Surg.* 2009;36:112–117.
9. Bombien R, Hümme T, Schünke M, Lutter G. Percutaneous aortic valve replacement: computer tomography scan after valved stent implantation in human cadaver hearts. *Eur J Cardiothorac Surg.* 2009;36:592–594.
10. Wendt D, Müller W, Hauck F, et al. In vitro results of a new minimally invasive aortic valve resecting tool. *Eur J Cardiothorac Surg.* 2009;35: 622–627.
11. Demming S, Quaden R, Leester-Schädel M, et al. Percutaneous aortic valve resection: evaluation of different micro actuator systems. In: *Proceedings of the International Society for Minimally Invasive Cardiothoracic Surgery*, Rome, Italy, June 6–9, 2007.
12. Bleiziffer S, Ruge H, Mazzitelli D, et al. Results of percutaneous and transapical transcatheter aortic valve implantation performed by a surgical team. *Eur J Cardiothorac Surg.* 2009;35:615–620.
13. Webb JG, Chandavimol M, Thompson CR, et al. Percutaneous aortic valve implantation retrograde from the femoral artery. *Circulation.* 2006;14:113:842–850.
14. Walther T, Falk V, Borger MA, et al. Transapical aortic valve implantation in patients requiring redo surgery. *Eur J Cardiothorac Surg.* 2009;36:231–234.
15. Walther T, Dewey T, Borger MA, et al. Transapical aortic valve implantation: step by step. *Ann Thorac Surg.* 2009;87:276–283.
16. Mora B, Skhirtladze K, Dworschak M. Severe cerebral desaturation during anterior transapical beating heart aortic valve implantation. *Br J Anaesth.* 2009;102:891–892.
17. Kallenbach K, Karck M. [Percutaneous aortic valve implantation—contra.] *Herz.* 2009;34:130–139.
18. Strauch JT, Kuhn E, Haldenwang PL, Wahlers T. Pulmonary trunk perforation during transapical minimal invasive aortic valve replacement. *Eur J Cardiothorac Surg.* 2009;35:1094–1095.
19. Hein A, Kirschstein U. Navigated imaging for angiography—concept and calibration. In: *IEEE International Conference on Mechatronics and Robotics, Aachen, Germany*, September 13–15, 2004:1409–1414.
20. Brell M, Isken M, Hein A, et al. Advanced multisensor soft tissue navigation for the controlled guidance in intra-cardiac microsurgery, In: *Proceedings of the 11th World Congress on Medical Physics and Biomedical Engineering (WC2009), Munich, Germany*, September 7–12, 2009.

CLINICAL PERSPECTIVE

In this article, Bombien et al examine the feasibility of endovascular resection of aortic valves using four different dissection systems. The resections were performed on seven human and 21 porcine hearts using a Thulium:YAG laser. The authors examined resection time and collateral damage. Their analysis demonstrated that their resection system with the newly designed nitinol (NiTi) microactuator that controlled the laser fiber with four degrees of freedom significantly reduced resection time and resulted in minimal collateral damage. This technology may be another step in decreasing the invasiveness of standard aortic valve replacement. However, the reader is to be cautioned that this is still preliminary, and it is difficult to assess the precise clinical utility of these systems without more realistic models. In comparing the different resection systems, each were investigated under different experimental conditions and even in different experimental models. This makes comparison difficult. Moreover, these valves were not highly calcified as can be seen clinically, and the utility of these systems in heavily calcified thickened pathologic valves remains to be demonstrated. Finally, these devices require a bloodless environment for visualization, which is a significant drawback to their utility in a minimally invasive environment. We await further progress from this group in the development of endovascular and endocardiac resection technology.

AUTHOR QUERIES

AUTHOR PLEASE ANSWER ALL QUERIES 1

1—Please note the given short title has been shortened further. Kindly confirm if this is OK.

2—Kindly provide the highest educational qualification obtained by the authors "Lesche," "Feucker," and "Sch¨unke."

3—Please note that the figure citations given in the Abstract have been deleted.

4—Kindly check whether the sentence "Second, the resection system…" is OK as edited.

5—Please check the phrase "fiber optic to a digital camera" in this sentence.

6—Please spell out "CT" in the text.

7—Please note that per journal style, Ref. 21 has been deleted from the list and incorporated in the text.

8—Please confirm whether the section heads are OK as intended.