

Article

Intraocular Lens Fragmentation Using Femtosecond Laser: An In Vitro Study

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Received: 3 February 2015

Accepted: 26 April 2015

Published: 12 June 2015

Keywords: intraocular lens explantation; cataract surgery; lens transection; hydrophilic acrylic lens; hydrophobic acrylic lens

Citation: Bala C, Shi J, Meades K. Intraocular lens fragmentation using femtosecond laser: an in vitro study. *Trans Vis Sci Tech.* 2015;4(3):8, doi:10.1167/tvst.4.3.8

Purpose: To transect intraocular lenses (IOLs) using a femtosecond laser in cadaveric human eyes. To determine the optimal in vitro settings, to detect and characterize gasses or particles generated during this process.

Methods: A femtosecond laser was used to transect hydrophobic and hydrophilic acrylic lenses. The settings required to enable easy separation of the lens fragment were determined. The gasses and particles generated were analysed using gas chromatography mass spectrometer (GC-MS) and total organic carbon analyzer (TOC), respectively.

Results: In vitro the IOL fragments easily separated at the lowest commercially available energy setting of 1 μ J, 8- μ m spot, and 2- μ m line separation. No particles were detected in the 0.5- to 900- μ m range. No significant gasses or other organic breakdown by products were detected at this setting. At much higher energy levels 12 μ J (4 \times 6 μ m spot and line separation) significant pyrolytic products were detected, which could be harmful to the eye. In cadaveric explanted IOL capsule complex the laser pulses could be applied through the capsule to the IOL and successfully fragment the IOL.

Conclusion: IOL transection is feasible with femtosecond lasers. Further in vivo animal studies are required to confirm safety.

Translational Relevance: In clinical practice there are a number of large intraocular lenses that can be difficult to explant. This in-vitro study examines the possibility of transecting the lenses quickly using femtosecond lasers. If in-vivo studies are successful, then this innovation could help ophthalmic surgeons in IOL explantation.

Introduction

Cataract surgery outcomes have greatly benefited from interference-based biometry, refinements in intraocular lens (IOL) power calculations and the development of foldable IOLs. Unfortunately, there are occasions when despite an uncomplicated cataract surgery lenses may need to be explanted, the reasons include incorrect power, opacification or dysphotopsia.^{1–12} Explantation of an IOL risks zonular dialysis, capsular tear, endothelial damage, and astigmatism depending on the corneal wound.

A number of strategies are currently used to explant lenses such as, cutting with scissors, folding in the anterior chamber or explanting as a whole.^{3,13–24} Scissors are available that allow lenses such as the

Acrysof (SN60WF; Alcon, Fort Worth, TX) to be cut and removed through small corneal incisions, avoiding induction of astigmatism.²⁰ These lenses lend themselves to cutting, as they are relatively thin owing to their high refractive index (1.5542). For example, a 22-diopter (D) lens SN60wf measures 0.633 mm at its thickest.

In comparison newer premium IOLS such as the Mplus (LU-313 MF30; Oculentis, Eerbeek, The Netherlands), which provide good visual outcomes are thicker and larger.^{25–29} These hydrophilic asymmetric refractive multifocal IOLs (with hydrophobic coating) have a refractive index of 1.461 and have a plate haptic design (6.0-mm optic and 11-mm plate haptic). A 22-D Mplus (LU-313 MF30; Oculentis) measures 1.04 mm at its thickest, which is a one-third

thicker than the equivalent hydrophobic Acrysof (SN60WF; Alcon) lens. Commercially available scissors cannot easily reach across the width of such a thick lens. Larger scissors require larger corneal incisions; risk trauma to the capsule and furthermore, the lens often pivots along the long axis of the scissor during the manoeuvre. Smaller scissors avoid these problems but owing to the large size of the IOL, a number of smaller cuts are required, which prolongs the procedure and risks trauma to the endothelium. These lenses are too large to fold in the anterior chamber and explant. Removing this lens as a whole is possible but would require a large corneal wound and could result in astigmatism in a patient where a premium IOL has been chosen.

Lastly, lens technology is changing rapidly and it is likely that multipiece lenses that provide accommodation may become available.³⁰ These could also prove to be a challenge to explant.

Femtosecond lasers platforms can perform many steps during cataract surgery including lensotomy and corneal wounds, but currently none offer IOL fragmentation.^{2,3} In this pilot study we explore the possibility of IOL fragmentation using the LenSx (Alcon) on hydrophobic (Acrysof IQ, SN60WF; Alcon) and hydrophilic (Mplus, LU-313MF30; Oculentis) acrylic IOLs prior to explantation.

Methods

The present study has the approval of the Human Ethics Committee of Macquarie University.

The Acrysof IQ (SN60WF; Alcon) and Mplus (LU-313 MF30; Oculentis) IOLs were placed between two single-well microscope slides (clear glass, 26 × 76 mm slide, 1.2- to 1.3-mm thick) and immersed in MilliQ water. The LenSx (version 2.23; Alcon) laser was docked and a linear 6-mm laser pattern was ablated using various settings (Fig. 1) to cover the sagittal profile of the IOL. At the present, the LenSx software does not allow for the IOL ablation to precisely match the sagittal profile of the IOL. This would require an alteration in the proprietary software. The authors do not have any commercial interests, and therefore this was not requested from the femtosecond manufacturer. Using the existing software, the minimum depth required for passing through the entire thickness of the IOL was 1.3 to 1.5 mm. One of the authors (CB) through trial and error determined the laser setting at which least mechanical force was required to separate the fragments.

Liquid Gas Chromatography

Six Acrysof IQ (SN60WF; Alcon), six Mplus (LU-313 MF30; Oculentis) IOLs, and six controls (without lens, only viscoelastic) jars were treated with a 6-mm linear femtosecond laser pattern at 1- and 12- μ J energy on a metal trephine in a 60-mL glass jar (product number 320-0060; Thermo Scientific). Immediately after laser application the gas jar was covered.

Thirty millilitres of liquid was sampled, mixed with 2 mL analytical grade hexane (Sigma), and the top 1.5 mL hexane was then transferred into GC-MS vials for further analysis. Shimadzu GC-MS Instrument (GC model: GC-2010 Plus with column RTX-5 MS; MS Model: MS QP 2010 Ultra) was used with the operation condition as follow: column oven operates from 40° to 250°C at a ramp rate of 10°C/min and the gases were identified with mass spectroscopy.

Total Organic Carbon

This is a well-established technique for measuring water purity by measuring the amount of carbon bound in an organic compound. This technique was used in the present study as IOLs are organic polymers and their fragmentation products should also be organic compounds. Three Acrysof IQ (SN60WF; Alcon), three Mplus (LU-313 MF30, Oculentis) IOLs, and three control (no lens, only viscoelastic) jars were treated with the femtosecond laser in a manner described above. The lens fragments were separated in the jar and the samples were processed for detection of particles. A Shimadzu TOC analyser (Model: TOC-L) with an auto-sampler (Model: ASI-L) was used to detect organic by-products generated in the laser fragment process. The TOC-L TOC analyser has a detection limit of 4 μ g/L¹ and was set to detect nonpurgeable organic carbon (NPOC) of 0.5 to 900 μ m.

A cadaveric human eye from which the cornea had been used for keratoplasty was obtained from the eye bank. The donor and their family's consent had been obtained for use of tissue for research by the eye bank. The lens capsular bag complex was removed. Viscoelastic was injected under the anterior capsule to allow mobilisation of the IOL in the capsular bag. The IOL-capsular bag complex with the viscoelastic was placed between the slides and subjected to femtosecond ablation. The tissue in total was returned to the eye bank on completion of the study.

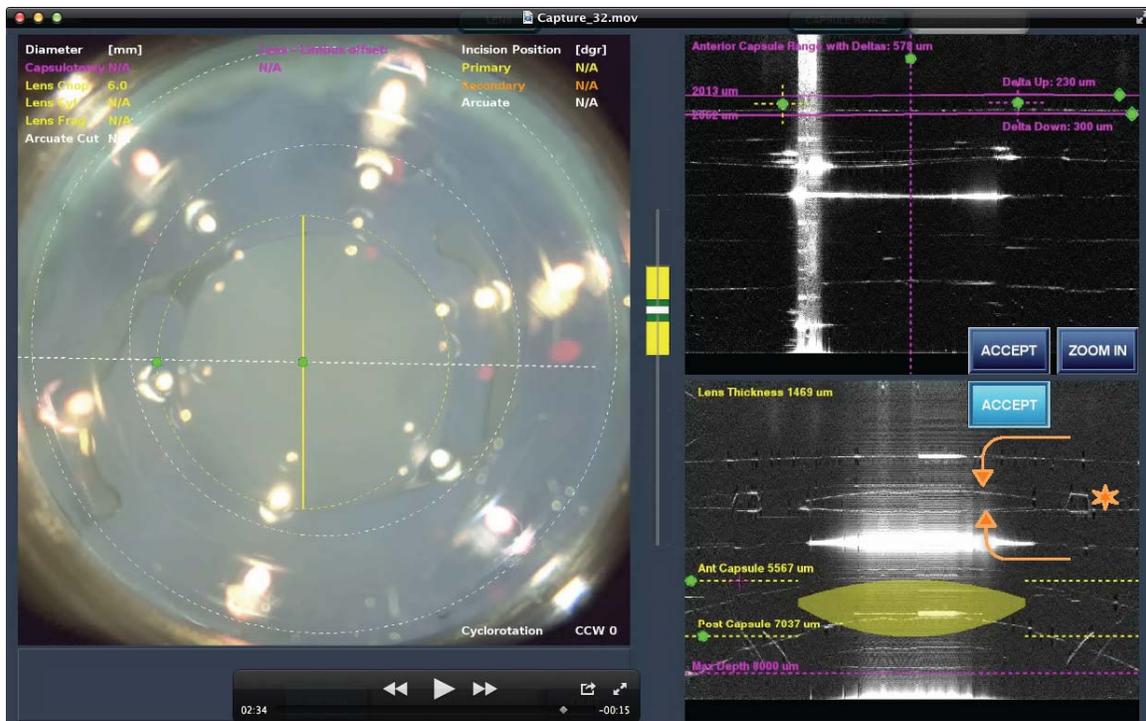


Figure 1. LenSx screen capture of IOL between glass slides prior to fragmentation. Star marks the sagittal OCT profile of the IOL. Arrows mark inner surfaces of the upper and lower slides.

Results

The hydrophobic (Acrysof IQ, SN60WF; Alcon) and hydrophilic (Mplus, LU-313 MF30; Oculentis) acrylic IOLs absorbed the femtosecond laser pulses and could be fragmented. The ‘optimal’ settings allowing relatively easy separation of fragments were 1 μ J, 8- μ m spot, and 2- μ m line separation. One microjoule was the lowest commercially available LenSx energy setting. Higher energy settings resulted in easier fragment separation but caused charring. Higher and lower spot separation (Fig. 2) were tried, with optimal separation at 8- μ m spot (S) and 2- μ m line (L) separation. Figure 3 shows the Acrysof IQ (SN60WF; Alcon) IOL fragments separated with greater charring at higher energy levels. The Mplus (LU-313 MF30; Oculentis) IOL, due to a lack of chromophore could not be photographed to show the effects of higher energy.

The duration of laser varied between depending on the layer and spot separation. For a cut 6-mm wide and 1.5-mm deep the duration varied from 15 seconds for 8 \times 2 to 11 seconds for 8 \times 3 to 14 seconds for 9 \times 2.

TOC analysis did not detect any significant increase (analysis of the variance; $P = 0.36$) in particles between the control samples (0.452 mg/L), hydrophobic Acrysof IQ (0.5052 mg/L; SN60WF; Alcon), and hydrophilic Mplus (0.364 mg/L; LU-313 MF30; Oculentis) lenses.

Gases are generated during laser IOL fragmentation. At higher energy levels 12 μ J (E), (8 μ m [S], 2 μ m [L]) the Acrysof IQ (SN60WF; Alcon) IOL (Fig. 4A) generated two gasses that comprised 90% of the total material extracted; 2-Propenoic acid 2-phenylethyl ester (Chemical Abstract Service [CAS] No. 3530-36-7) and 2-Propenoic acid 2-methyl-2-phenylethyl ester (CAS No. 3683-12-3). The remaining gasses were Styrene (CAS No. 100-42-5), phenylethyne (CAS No 536-74-3), benzene (CAS No. 71-43-2), and Ethylbenzene (CAS No. 100-41-4).

The Mplus (LU-313 MF30; Oculentis) hydrophobic IOL (Fig. 4B) at 12 μ J, (8 μ m [S] \times 2 μ m [L]) generated mainly 2-Ethoxyethyl Methacrylate (CAS No 2370-63-0). Other gasses generated included: Styrene (CAS No 100-42-5), Phenylethyne (CAS No 536-74-3), Benzene (CAS No 71-43-2), Toluene (CAS No 108-88-3), and Ethylbenzene (CAS No 100-41-4). Lowering the energy to 1 μ J resulted in no significant

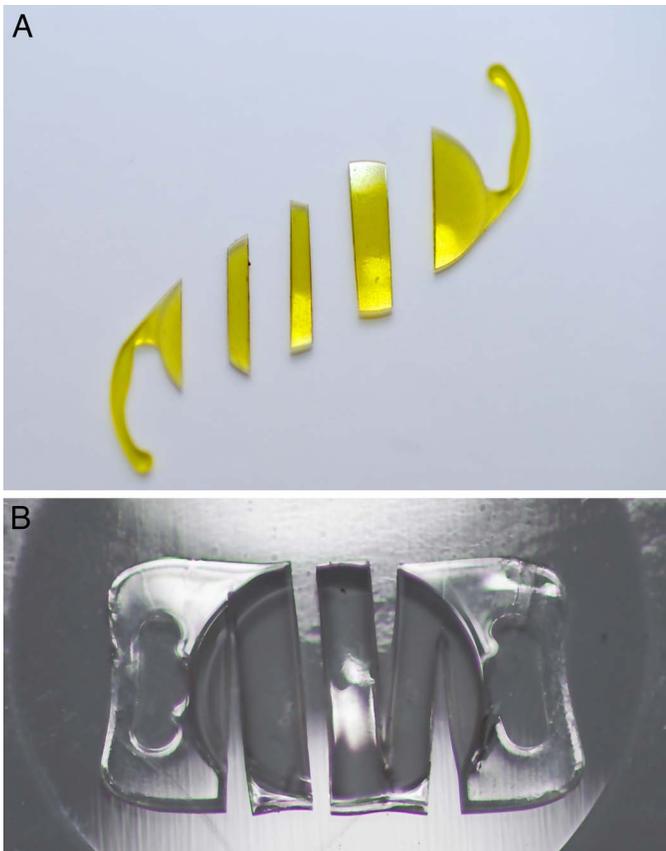


Figure 2. (A) Cut fragments of hydrophobic acrylic lens. (B) Cut fragments of hydrophilic acrylic lens. From *left to right* the settings (energy \times spot separation, line separation) for each fragmentation for both lenses were $1 \mu\text{J} \times 8 \mu\text{m} \times 2 \mu\text{m}$, $2 \mu\text{J} \times 8 \mu\text{m} \times 2 \mu\text{m}$, $1 \mu\text{J} \times 8 \mu\text{m} \times 3 \mu\text{m}$, and $1 \mu\text{mJ} \times 9 \mu\text{m} \times 2 \mu\text{m}$.

gasses being detected with either of the lenses (Fig. 4C).

In a cadaveric human eye, the IOL capsular complex was removed. The IOL was successfully fragmented while in the bag (Fig. 5) with an intact anterior and posterior capsule.

Discussion

Femtosecond lasers when passed through a transparent medium can act as an internal scalpel.

In the present in vitro study, it has been demonstrated that fragmentation of the IOL is possible with the femtosecond laser. It is not surprising that no particles were detected as the Femtosecond laser raises the temperature at its point of application and causes pyrolysis.

The basic atomic components of all lenses are



Figure 3. Cut edge of Acrysof IQ (Sn60wf) lens showing increased charring at the higher energy levels. Left most edge was generated using the settings $1 \mu\text{J} \times 8 \mu\text{m} \times 2 \mu\text{m}$ (energy \times spot separation, line separation). The second and third edges were generated with $2 \mu\text{J} \times 8 \mu\text{m} \times 2 \mu\text{m}$ and show mirror charring of lens edge. The *right most edge* was generated using $1 \mu\text{mJ} \times 9 \mu\text{m} \times 2 \mu\text{m}$.

carbon, hydrogen, and oxygen, making them organic entities. The Acrysof IQ (SN60WF; Alcon) hydrophobic lens is made of a copolymer of acrylate and methacrylate. The Mplus (LU-313 MF30; Oculentis) hydrophilic acrylic lenses have hydroxyethyl-methacrylate and a hydrophilic component. The femtosecond laser energy breaks the covalent bonds at different locations depending on the energy used.

At higher energies, the gases generated of greatest concern are, Styrene, Phenylethyne, Benzene, Toluene, and Ethylbenzene. The risk associated with these would depend on the amount and duration of exposure and have not been determined in ophthalmology. The US Department of Health and Human Service categorises Benzene as a human carcinogen, and Toulene and Styrene are reasonably anticipated to be carcinogenic.³¹ The US Environmental Protection Agency recommends maximum levels in drinking water to be Benzene 5, Styrene 100, and Toulene 1000 $\mu\text{g/L}$.³² The present study did not measure the amount generated in solution but only detected the presence of gasses, as there was some loss to the atmosphere from the time of laser application to the laser gantry being removed and the glass jar being capped.

In the present study, at low energy settings toxic gasses were not detected presumably due to lower temperature rise. It is possible that not all the gas was captured; this can be addressed with an in vivo animal study looking at endothelial damage from femtosecond laser and collecting gasses from a confined space such as an anterior chamber.

The in vitro fragmentation was easily performed at the commercially available minimum laser energy of $1 \mu\text{J}$. It is possible that energies lower than $1 \mu\text{J}$ could achieve the same result. This should further reduce the danger of producing toxic gasses. The energy setting used cannot be extrapolated to in vivo settings,

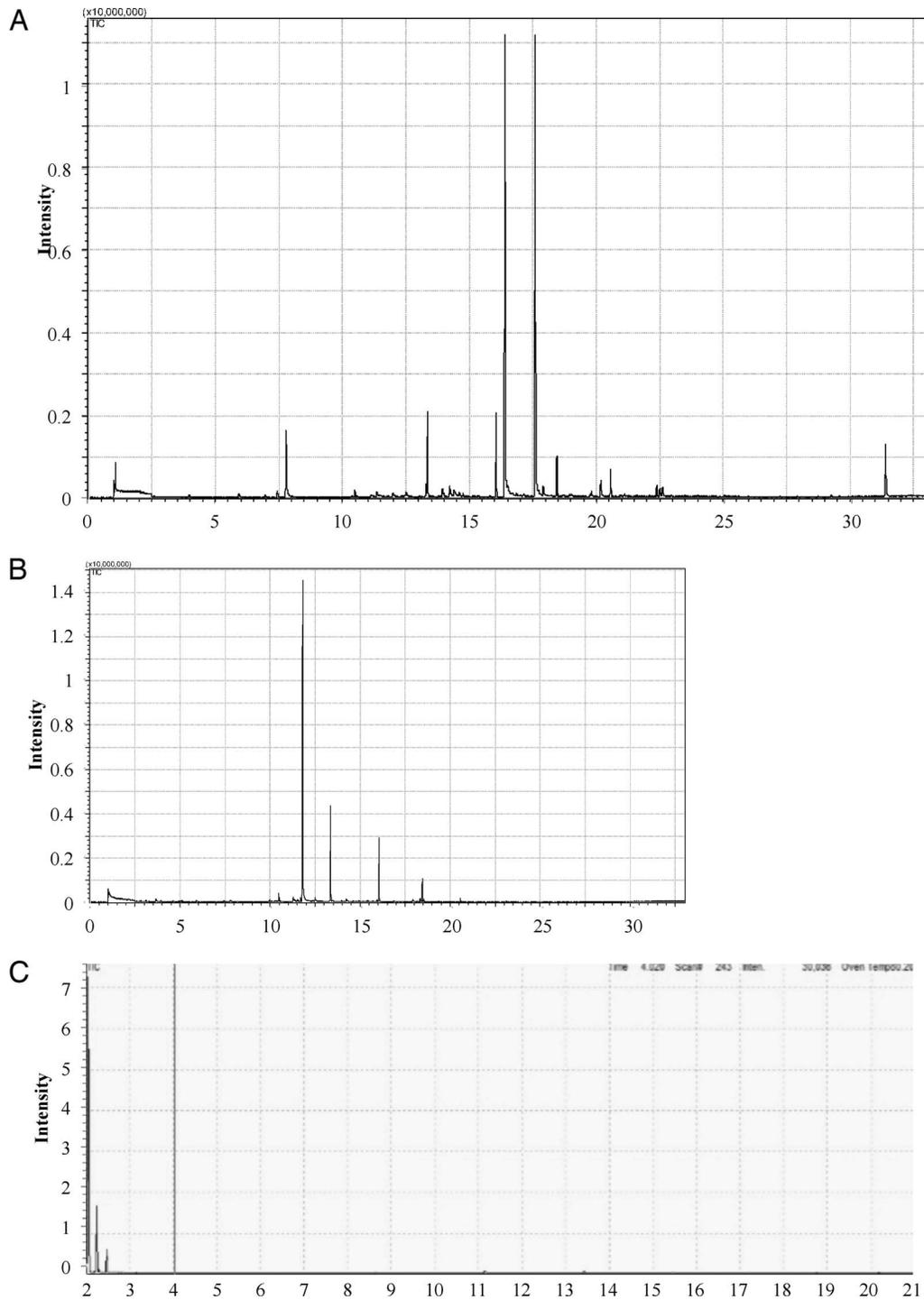


Figure 4. Spectrum of gases detected by gas chromatography following transection of hydrophobic acrylic and hydrophilic acrylic lenses using two different energy levels. (A) The transection of Acrysof SN60wf at 12 μJ generates a number of gasses listed in the text. (B) Different gases are generated with the transection of hydrophilic lenses at 12 μJ . (C) No gasses were detected with the transection of the lenses at 1 μJ . Peaks to the *left* of the graph relate to the hexane solvent used to extract the gas for liquid gas chromatography (namely cyclohexane, cyclopentane, and heptane). The x-axis represents time in minutes.



Figure 5. Transection of IOL through the capsule in an explanted cadaveric human IOL-lens capsular bag complex. The IOL was fragmented through the bag and shows an intact anterior lens capsule stained with vision blue.

as the cornea and aqueous will affect transmission. These would have to be reassessed.

Performing IOL fragmentation in the capsular bag risks bag perforation and also the possibility of not being able to mobilize the cut IOL due to capsular adhesions. In the present study, viscoelastic was injected posterior to the IOL in the cadaveric IOL-bag complex. The femtosecond laser was successful in passing through the capsule and cutting the IOL. In vivo an alternate strategy would be to mobilize the lens and explant half the lens into the anterior chamber prior to laser fragmentation. The fragments could then be removed through a small corneal incision. The viscoelastic would also trap the gas limiting exposure to the corneal endothelium. It should also be noted that this procedure would require sterile docking. In the past femtosecond laser cataract surgery has been performed following the insertion of a pupil expander and therefore it may be possible to perform IOL fragmentation in the same manner.³³ At the present, the Lensx software does not allow for the IOL ablation to exactly match the profile of the IOL. This would require an alteration in the software of the laser platform.

Currently, there are a number of instruments that can transect IOLs and allow safe removal through small incisions. There are however, hydrophilic IOLs that have thick optics, such as the Mplus (LU-313 MF30; Oculentis) tested here which are difficult to transect. If this procedure is safely performed in animal studies, it may allow easier explantation/exchange of such IOLs. Fragments could be removed

through small incisions and relatively quickly without significant ocular trauma resulting in quicker recovery. Further studies will also be needed to see if the cost of the femtosecond laser fragmentation will be offset by the quicker recovery of the patient.

Acknowledgments

The authors thank Christopher McRae of Mcquarie University.

Disclosure: **C. Bala**, None; **J. Shi**, None; **K Meades**, None

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