

Centre universitaire
de santé McGill



McGill University
Health Centre

**Technology Assessment Unit of the McGill
University Health Centre (MUHC)**

Excimer laser atherectomy for uncrossable coronary lesions and improperly deployed coronary stents

Report number: 75

DATE: June 9, 2014

Report available from <http://www.mcgill.ca/tau>

**Report prepared for the Technology Assessment Unit (TAU)
of the McGill University Health Centre (MUHC)**

by

Alison Sinclair, Nandini Dendukuri

Requested by: Mr. Gary Stoopler, Administrative Director,
Medical Mission, McGill University Health Centre

Approved by the Committee of the TAU on June 9, 2014

TAU Committee

**Andre Bonnici, James Brophy, Nandini Dendukuri,
Sandra Dial, Christian Janicki, Patricia Lefebvre,
Brenda MacGibbon-Taylor, Gary Pেকেles, Guylaine Potvin,
Patty O'Connor, Hugh Scott**

Suggested citation:

Sinclair A., Dendukuri N. Excimer laser atherectomy for uncrossable coronary lesions and improperly deployed coronary stents. Montreal (Canada): Technology Assessment Unit (TAU) of the McGill University Health Centre (MUHC); 2014 June 9, Report no. 75. 28 p.

Available from:

<http://www.mcgill.ca/tau/publications>

ACKNOWLEDGEMENTS

The expert assistance of the following individuals is gratefully acknowledged:

- Dr. Luc Bilodeau, Director of the Cardiac Catheterization Laboratory, Cardiovascular Division of the Department of Medicine
- Dr. Maurice McGregor of the Technology Assessment Unit

- We thank Dr. Alain Lapointe, external consultant, for French translation of our abstract and executive summary.

TABLE OF CONTENTS

| | |
|---|-----|
| Acknowledgements | i |
| Table of contents..... | ii |
| List of tables | iii |
| List of figures..... | iii |
| Abstract | iv |
| Résumé..... | v |
| List of abbreviations | vi |
| Executive summary | vii |
| Sommaire..... | ix |
| Background..... | 1 |
| Objectives | 2 |
| Methods | 2 |
| Literature search and quality assessment..... | 2 |
| Meta-analysis..... | 3 |
| Cost analysis | 3 |
| Literature review..... | 3 |
| Health technology assessments | 3 |
| Observational studies | 4 |
| Summary | 6 |
| Ongoing randomized controlled trials..... | 7 |
| ELCA at the MUHC | 7 |
| Budget impact..... | 7 |
| Discussion..... | 7 |
| Conclusions..... | 8 |
| Recommendations | 9 |
| Tables | 10 |
| References..... | 14 |

LIST OF TABLES

| | | |
|---------|--|----|
| Table 1 | Studies using excimer laser atherectomy in patients with uncrossable lesions, chronic total occlusions and underexpanded stents: Study descriptions..... | 10 |
| Table 2 | Studies using excimer laser atherectomy in patients with uncrossable lesions, chronic total occlusion and underexpanded stents: Study results | 12 |

LIST OF FIGURES

| | | |
|----------|--|---|
| Figure 1 | Summary of procedural success without major AEs for studies of excimer laser atherectomy in patients with uncrossable lesions/ chronic total occlusions..... | 6 |
|----------|--|---|

ABSTRACT

Balloon angioplasty with stent implantation is a standard treatment for symptomatic coronary artery lesions. Two reasons for failure of this procedure are inability to penetrate a complete coronary occlusion and failure to adequately expand the stent.

Evidence of the effectiveness and safety of attempting to correct these problems using current models of excimer laser is restricted to case series. Most report a fairly high rate of successful procedures and a low but not insignificant complication rate. Information on outcomes observed during follow-up is limited to one observational study (6 months). There is no evidence to support a conclusion that a successful procedure improves symptoms over time or extends life.

Assuming that this intervention does not necessitate an additional catheterization procedure, the cost to the MUHC would be \$1500 per patient.

The present evidence of benefit of this procedure is insufficient to justify the associated opportunity cost for routine clinical use. Further investigation of this technology should be considered and funded as a research procedure.

RÉSUMÉ

L'angioplastie par ballonnet avec implantation d'une endoprothèse ("stent") est un traitement classique pour les lésions symptomatiques des artères coronaires. Deux raisons peuvent expliquer l'échec de cette procédure, soit l'incapacité à traverser une occlusion coronarienne complète ainsi que l'incapacité à déployer adéquatement l'endoprothèse.

Les preuves de l'efficacité et de l'innocuité des tentatives pour corriger ces problèmes en utilisant les modèles actuels de laser excimer sont limitées aux séries de cas. La plupart rapportent un taux assez élevé de procédures réussies ainsi qu'un faible mais significatif taux de complications. L'information relative aux résultats observés pendant le suivi se résume à une étude observationnelle pendant une période de 6 mois. Il n'y a aucune preuve supportant la conclusion que la réussite de cette procédure améliore les symptômes dans le temps ou prolonge la vie.

Si l'on assume que cette intervention ne nécessite aucun cathétérisme supplémentaire, le coût imputable au CUSM (Centre universitaire de santé McGill) serait de 1 500 \$ par patient.

Les preuves actuelles des bénéfices de cette procédure sont insuffisantes pour justifier le coût d'opportunité qui en découle, pour un usage clinique de routine. La poursuite de l'étude de cette technologie devrait être considérée et financée comme une procédure de recherche.

LIST OF ABBREVIATIONS

| | |
|--------|--|
| AE | Adverse event |
| CADTH | Canadian Agency for Drugs and Technologies in Health |
| CRD | Centre for Research and Dissemination |
| CTO | Chronic total occlusion |
| DARE | Database of Abstracts of Reviews of Effects |
| ELCA | Excimer laser coronary atherectomy |
| EMBASE | Excerpta Medica Database |
| INAHTA | International Network of Agencies for Health Technology Assessment |
| INESSS | L'Institut national d'excellence en santé et en services sociaux |
| MUHC | McGill University Health Centre |
| NICE | National Institutes for Health and Clinical Excellence |
| QALY | Quality adjusted life-year |
| RCT | Randomized controlled trial |
| TAU | MUHC Technology Assessment Unit |
| MUHC | McGill University Health Centre |

EXECUTIVE SUMMARY

Background

Balloon angioplasty and stent implantation is standard treatment for symptomatic coronary artery lesions. Atherectomy, whether by mechanical means or laser, has not been found to improve long-term outcomes over standard treatment in the majority of patients. The TAU was asked to review the use of excimer laser for atherectomy using the Spectranetics CVX-300 xenon-chlorine excimer laser and associated catheters in two specific uncommon situations: i) in which the deflated balloon could not pass through the lesion (uncrossable lesion, <1% of lesions), and ii) in which an implanted stent did not expand to its full diameter (improperly deployed/underexpanded stent, <5% of lesions).

Method

A systematic literature search of PubMed, MEDLINE and EMBASE (Ovid), Cochrane, CRD databases, and HTA websites was carried out using “coronary” as a text-word, and general and specific terms for the intervention. We screened articles for the specific lesions of interest and for use of the xenon-chlorine excimer laser. As well as articles on uncrossable lesions, we reviewed material on chronic total occlusions (CTOs), a subset liable to have a significant overlap. The search was last updated on February 4, 2014.

Results: Literature review

Health technology assessments A 2010 NICE review concluded that the evidence was adequate to support the use of excimer laser coronary atherectomy (ELCA) in carefully selected patients for whom conventional angioplasty would be technically difficult, provided institutional controls were in place.

Review of evidence on balloon-uncrossable lesions Four case series included 36 patients with balloon-uncrossable lesions and an additional 108 patients with CTO. Rates of clinical success (procedural success with no major adverse events) ranged from 64% (for ELCA alone) to around 90% for ELCA with and without rotational atherectomy. There was one laser-related peri-procedural fatality due to perforation, and reported perforation rates were 0-3.4%. Other peri-procedural adverse events included coronary artery dissection (per-study rate, 0-9.3%), myocardial infarction (0-10.4%), and major bleeding (0-6.2%). One study (2003) reported on six month follow-up for 46 patients with CTO. For those who successfully underwent the procedure, event-free survival was 76%, 9 (19.5%) underwent repeat angioplasty, and one underwent coronary artery bypass grafting.

Review of evidence on underexpanded stents of 28 patients in one case series of patients with underexpanded stents, all but one had procedural success, with no deaths and one MI. In 6-month follow-up, one patient with pre-existing severe LV dysfunction died suddenly; other long term outcomes were not reported.

ELCA at the MUHC

ELCA has not previously been used at the MUHC; however it has previously been used by the local expert, Dr. Luc Bilodeau. It is estimated that it may be used for approximately 10 patients per year.

Costs

An estimated 10 patients would undergo ELCA annually, and would result in an additional cost to the MUHC of between \$15,000 (for catheters alone, assuming no additional procedures) and \$80,000 (assuming all additional procedures).

CONCLUSIONS

- **The overall benefit of angioplasty with stent implantation is established, However, failure may result in two small sub-groups of patients; those with uncrossable lesions and those with underexpanded stents.**
- **Evidence for the use of excimer laser atherectomy using current technology for these two indications is restricted to case series. Most of these report a fairly high rate of procedural success, but information on outcomes during follow-up is limited to one observational study (6 months).**
- **There is no evidence to support a conclusion that a successful procedure leads to symptomatic improvement or increased longevity.**
- **Reported serious adverse events are not infrequent. In a total of 261 proceduresⁱ, one patient died as a result of perforation. Per-study rates of coronary artery dissection were 0-9.3%, myocardial infarction, 0-10.4%, and major bleeding, 0-6.2%.**
- **The additional cost to the hospital for 10 patients per year would be between \$15,000 (assuming no additional procedures) and \$80,000 (assuming all are additional procedures).**

RECOMMENDATIONS

The present evidence of benefit of this procedure is insufficient to justify the associated opportunity cost. It could be considered only as a fully funded research activity.

ⁱ These were not all uncrossable lesions or underexpanded stents, as some studies included several types of complex lesions and did not report results separately.

SOMMAIRE

Contexte

L'angioplastie par ballonnet et l'implantation d'une endoprothèse ("stent") est un traitement classique pour les lésions symptomatiques des artères coronaires. L'athérectomie, effectuée par un moyen mécanique ou par laser, ne semble pas améliorer les résultats à long terme par rapport au traitement classique chez la majorité des patients. L'Unité d'évaluation des technologies ("Technology Assessment Unit") fut sollicitée pour revoir l'utilisation du laser excimer pour l'athérectomie au moyen du laser excimer xénon-chlore Spectranetics CVX-300 avec les cathéters appropriés, lors de deux situations précises peu fréquentes: i) lorsque le ballonnet non-gonflé ne peut passer à travers la lésion (lésion infranchissable, <1% des lésions) et ii) lorsque l'endoprothèse implantée ne s'est pas déployée à son diamètre maximum (endoprothèse incorrectement déployée/sous-déployée, <5% des lésions).

Méthodologie

Une recherche systématique de la littérature fut menée à partir des bases de données Pubmed, MEDLINE, EMBASE (Ovid), Cochrane, CRD databases et des sites Internet d'évaluation des technologies ("HTA") en utilisant le mot "coronary" ainsi que des termes généraux et spécifiques pour cette intervention. Nous avons filtré les articles pour retenir ceux touchant spécifiquement les lésions d'intérêt et mentionnant l'utilisation du laser excimer au xénon-chlore. Nous avons aussi revu les articles sur les occlusions totales chroniques (OTC) ainsi que ceux traitant des lésions infranchissables, un sous-groupe susceptible de montrer un chevauchement important. La dernière mise à jour de cette recherche fut faite le 4 février 2014.

Résultats. Revue de la littérature

Évaluation des technologies

Une revue faite par l'organisme NICE et publiée en 2010 a conclu que les preuves étaient valables pour supporter l'athérectomie coronarienne par laser excimer (ACLE) chez les patients soigneusement choisis chez qui l'angioplastie conventionnelle serait techniquement difficile, à la condition que les contrôles institutionnels soient en place.

Revue des preuves relatives aux lésions infranchissables par ballonnet

Quatre séries de cas comportaient 36 patients présentant des lésions infranchissables par ballonnet de même que 108 patients supplémentaires avec une OTC. Les taux de réussite clinique (réussite de la procédure sans événement indésirable majeur) s'échelonnaient de 64% (pour l'ACLE seule) à environ 90% pour l'ACLE, avec et sans athérectomie rotationnelle. Un décès péri-procédural fut rapporté dû à une perforation. Le taux de perforation rapporté variait de 0 à 3,4%. Les autres événements indésirables lors de la procédure comprenaient la dissection

de l'artère coronaire (taux par étude, 0-9,3%), l'infarctus du myocarde (0-10,4%) et les saignements majeurs (0-6,2%). Une étude publiée en 2003 présentait le suivi de 6 mois chez 46 patients avec une OTC. Pour les patients chez qui la procédure fut un succès, le taux de survie sans événement indésirable était de 76%, 9 patients (19,5%) subirent des angioplasties répétées et un patient dut subir un pontage aorto-coronarien.

Revue des preuves pour les endoprothèses sous-déployées

Dans une série de cas de 28 patients avec des endoprothèses non-déployées, tous les patients, sauf un, subirent avec succès cette procédure; aucun décès ne fut rapporté, à l'exception d'un infarctus myocarde. Lors d'un suivi de 6 mois, un patient avec une dysfonction ventriculaire gauche sévère déjà présente est mort subitement; d'autres résultats à long terme n'ont pas été rapportés.

ACLE au CUSM

L'ACLE n'a pas encore été utilisée au CUSM; cependant, cette procédure a déjà été utilisée par le Dr Luc Bilodeau, médecin spécialisé au CUSM. Selon un estimé, cette procédure pourrait être réalisée chez environ 10 patients par année.

Les coûts

Si l'on estime que 10 patients pourraient subir une ACLE annuellement, le coût supplémentaire pour le CUSM varierait entre 15 000 \$ (incluant seulement les cathéters, sans procédures supplémentaires) et 80 000 \$ (en tenant compte de toutes les procédures supplémentaires).

CONCLUSIONS

- De façon générale, les bénéfices de l'angioplastie avec implantation d'une endoprothèse sont reconnus. Cependant, l'échec de cette procédure peut être observé chez deux petits sous-groupes de patients: ceux présentant des lésions infranchissables et ceux avec des endoprothèses sous-déployées.
- Les preuves supportant la procédure d'athérectomie par laser excimer en utilisant la technologie actuelle pour les deux indications précédentes, sont limitées aux séries de cas. La plupart de ces publications rapportent un taux assez élevé de réussite de cette procédure mais l'information sur les résultats lors du suivi se résume à une étude observationnelle de 6 mois.
- Il n'y a aucune preuve supportant la conclusion que la réussite de cette procédure se traduit par une amélioration des symptômes ou une augmentation de la longévité.
- La mention d'événements indésirables graves n'est pas rare. Pour un total de 261 procédures, un patient est décédé suite à une perforation. Les taux par étude de dissection des artères coronaires variaient de 0 à 9,3%, de 0 à

10,4% pour l'infarctus du myocarde et de 0 à 6,2% pour les saignements majeurs.

- Le coût supplémentaire pour l'hôpital pour 10 patients par année varierait entre 15 000 \$ (sans procédures supplémentaires) et 80 000 \$ (en tenant compte de toutes les procédures supplémentaires).

RECOMMANDATIONS

Les preuves des bénéfices découlant de cette procédure sont insuffisantes pour supporter le coût d'opportunité qui en découle. Elle ne pourrait être considérée que comme une activité de recherche entièrement financée.

Excimer laser atherectomy for uncrossable coronary lesions and improperly deployed coronary stents

BACKGROUND

Coronary artery disease is widespread, particularly in the aging population¹, and frequently requires intervention to restore adequate blood flow to the myocardium. Today the established percutaneous (as opposed to surgical) intervention involves balloon angioplasty of the coronary lesion, followed by implantation of a stent (bare metal or drug-eluting)¹.

However, historically there was an interest in atherectomy (or plaque removal) as an alternative intervention for treating coronary artery disease. Early randomized controlled trials compared plaque removal (either mechanically by means of a burr or by excimer laser) with balloon angioplasty. They showed no advantage to atherectomy in preventing restenosis in patients with unselected coronary lesions² or in-stent restenosis³, while increasing the risk of adverse events, e.g., perforation. There is, however, continuing interest in the use of laser atherectomy in certain specific indications, e.g., where the artery is too stenosed to allow the passage of even a deflated balloon, or where the stent does not deploy properly, even at maximum balloon pressure. In the latter case, attempted debulking of the lesion with mechanical atherectomy risks displacing the stent.

The Spectranetics CVX-300 xenon-chlorine excimer laser is a new generation xenon-neon laser designed to produce stronger ablation with lower heat and vessel wall disruption. This is used with the currently available catheter models, the ELCA Coronary Laser Atherectomy Catheter⁴, designed for coronary laser atherectomy, and the Turbo Elite laser atherectomy catheter⁵, primarily designed for treatment of peripheral vascular stenoses. The two models of catheter have similar designs (circular or eccentric, wire-exchangeable and over the wire), but the Turbo Elite delivers higher energy than the ELCA models, with the exception of the ELCA X-80.

The Technology Assessment Unit was requested by : Gary Stoopler, Administrative Director, Medical Mission, McGill University Health Centre and to review the evidence for excimer laser use in selected patients undergoing percutaneous coronary intervention for complicated lesions, specifically i) patients with balloon-uncrossable lesions (<1% of lesions)⁶, and ii) those with improperly deployed coronary stents (<5% of lesions)⁷. The former are generally found at the time of the initial procedure, while the latter may be observed either at the time of the initial procedure, or when symptoms recur. The request considers the cost of the catheters only (ELCA Coronary Laser Atherectomy Catheter), as the laser generator itself is available by previous arrangement between the MUHC and the manufacturers.

OBJECTIVES

The objectives of this health technology assessment report are to consider whether evidence on the effectiveness and safety of atherectomy by excimer laser is sufficient to justify its use at the MUHC, and to estimate the cost.

Use of this technology will be considered in two situations.

- Prior to balloon angioplasty and stent implantation in patients with uncrossable coronary lesions, or
- Following stent implantation in patients with underexpanded coronary stents.

METHODS

Literature search and quality assessment

We identified relevant reports and studies by searching electronic databases and websites, scanning citation lists of retrieved articles, and consultation with experts. For health technology assessments, economic assessments, and systematic reviews we searched CADTH (and CADTH confederated search), and databases at the Centre for Reviews and Dissemination, York. For systematic reviews and RCTs we searched the Cochrane Collaboration and Cochrane CENTRAL. For all study types we searched PubMed (1996 to 2014), MEDLINE (OVID) (1996 to February 3, 2014), and EMBASE (OVID) (1996 to February 3, 2014). Main search terms were “coronary” as a text-word, to capture the variable terms of reference to coronary artery lesions, and specific and general terms for the intervention (“CVX-300” and “xenon-chlorine”, and “excimer laser” as keywords and mapped to the relevant indexing term). To exclude the use of excimer laser in intervention in other vessels or in pacemaker lead extraction, we excluded papers that referred to other indications in the title. We did not attempt to limit the search by lesion type because of the risk of excluding papers in which the patients of interest were a subgroup. We did not limit the search by language, date, population or study type, although we excluded studies in languages other than English or French at the stage of full text review. The search was last updated on February 4, 2014. To identify studies in progress/unpublished studies, we searched ClinicalTrials.gov and Current Controlled Trials using keywords ‘coronary’ and ‘laser’.

We included randomized controlled trials, case series and case reports that included patients who underwent interventions involving excimer laser (Spectranetics CVX-300 xenon-chlorine laser) for uncrossable lesions or underexpanded stents. Only a minority of reports identified lesions as uncrossable, but we also retrieved papers on excimer laser atherectomy with stent placement in chronic total occlusions (CTOs), a subset liable to have a significant overlap with uncrossable lesions⁸.

For patients with uncrossable lesions, ELCA debulking would have preceded stent placement. For patients with underexpanded stents, ELCA debulking would have taken place with the stent in situ.

One author (AS) conducted the search, reviewed the search, and screened papers for inclusion.

Meta-analysis

Scoping search suggested that the evidence would be limited, and therefore no meta-analysis was planned.

Cost analysis

We calculated budget impact for a projected 10 patients at \$1500 per laser catheter. We could not anticipate how many of these cases would involve a repeat procedure made possible by the catheter (eg, delayed treatment of an underexpanded stent). We therefore calculated costs in two situations (a) the catheter is used as part of the initial procedure, and the only additional cost is the catheter, (b) the catheter is used in a repeat procedure, and the total cost is that of the repeat procedure including catheter.

LITERATURE REVIEW

In Section 4.1 below we summarize the results of recent health technology assessment. In Section 0 we describe evidence from individual studies and Section 0 presents an overall summary. In each section evidence is summarized separately for balloon-uncrossable lesions and for under-expanded stents.

Health technology assessments

We found a 2010 interventional procedures overview of percutaneous laser coronary angiography in *all lesion types*⁹ and accompanying interventional procedure guidance (January 2011)¹⁰ from NICE (UK).

From the results of a rapid review of databases including Cochrane, MEDLINE and PREMEDLINE and EMBASE, the authors of the NICE overview selected two meta-analyses^{2, 3} and two RCTs involving patients with CTO¹¹ and in-stent restenosis. Approximately 28,000 patients were involved, only a minority of whom had the lesions of interest. The reviewers concluded that,

Current evidence on the safety and efficacy of percutaneous laser coronary angiography is adequate to support the use of this procedure in carefully selected patients for whom conventional angioplasty would otherwise be technically difficult, provided that normal arrangements are in place for clinical governance, consent and audit¹⁰.

Observational studies

Study characteristics are summarized in Table 1 and patients and outcomes in Table 2.

Uncrossable lesions

We did not identify any RCTs using current technology. An earlier RCT using an excimer laser wire in chronic total occlusion¹¹ involved a model of laser guidewire that has since been abandoned due to high rate of perforation (Dr. Luc Bilodeau, personal communication). We found four case series^{6, 12-14} in English describing the use of excimer laser prior to stent placement in patients with lesions described as balloon-uncrossable or chronic total occlusions (Table 1 and Table 2).

Patients with balloon-uncrossable lesions

Fernandez et al, 2013¹⁴, collected a single-centre retrospective case series of 58 patients with coronary lesions treated with excimer laser (with or without rotational atherectomy) following balloon failure between 2007 and 2011. Thirty-six had balloon-uncrossable lesions and the remaining 22 patients had lesions resistant to balloon expansion. Of the patients with balloon-uncrossable lesions, 20 had CTO. The catheter used was a Vitesse C 0.9 mm catheter (Spectranetics).

Procedural success, defined as stent deployment with <20% residual stenosis and without major complications, was achieved with ELCA alone in 23/36 (63.9%) of patients with balloon-uncrossable lesions. Addition of cases in which ELCA and mechanical atherectomy were used in conjunction, or in which ELCA succeeded after failure of mechanical atherectomy, increased the procedural success rate to 31/36 (86.1%).

Among the patients with balloon-uncrossable lesions, one patient died of cardiogenic shock following a type III coronary artery perforation related to the laser catheter. One patient experienced occlusion of a side-branch without significant rise in cardiac enzymes, and one developed transient no-reflow at an area remote from the site of intervention. An additional Type I balloon-related perforation was reported for a patient with a non-expandable lesion. No follow-up data were reported.

Patients with chronic total occlusions

Badr et al, 2013¹³ reported on a single centre retrospective case series of 119 patients with 124 lesions treated by ELCA, of whom 32 had CTO. Angiographic success, defined as <50% residual stenosis after ELCA and adjunct therapy (balloon angioplasty), and clinical success, defined angiographic success and no major complications prior to discharge, was reported for 29/32 (90.6%) of the patients with CTO. There were five ELCA-related adverse events: three coronary dissections, one coronary perforation in a patient who subsequently underwent CABG, and one thrombus formation (location not specified). One patient required emergency intra-aortic balloon pump implantation and two suffered major bleeding (the report did not

relate these to the other listed adverse events). Again, follow-up did not extend beyond the periprocedural period.

An observational study involving 95 patients with 100 complex lesions compared standard with intensified laser therapy, and included 28 patients with CTO (Bilodeau et al, 2004⁶). Results for patients with CTO were not reported separately in the published paper. Overall rate of procedural success, defined as <50% residual stenosis after ELCA and adjunct therapy (balloon angioplasty), was 87/95 (92%). The combined rate of clinical success, defined angiographic success and absence of major adverse cardiac events prior to discharge, was 83/95 (86%). Adverse events in the 95 patients included 5 patients with dissection.

The third and earliest study of patients with CTO included 48 patients who underwent laser atherectomy and stent implantation (Babalik et al, 2003¹²). Rate of procedural success, defined as residual stenosis <50% without a major complication, was 46/48 patients (95.8%). Clinical success, defined as procedural success without myocardial infarction, need for repeat angioplasty or bypass surgery prior to discharge, was achieved for 41/46 patients (85.4%). During six month follow up for patients who had successfully undergone a procedure, one patient underwent a CABG, and nine (19.5%) had repeat balloon angioplasty. Overall event-free survival was 76%, and there were no deaths or MIs during that period.

Underexpanded stents

One registry study¹⁵ and seven case reports¹⁶⁻²² described the use of excimer laser to expand underexpanded stents.

The registry study (see Table 1 and Table 2) recruited 28 patients between 2009 and 2011, 3 of whom had recent implantation and 25 of whom had stenosis from a previous underexpanded implant. All patients had previously undergone unsuccessful balloon angioplasty directed at re-expanding the stent. The procedure used the Turbo Elite catheter 0.9 to 2.0 mm, with fluence up to 80 mJ/mm² and a pulse repetition rate up to 80Hz (similar to the X80 ELCA model), with contrast injection. All settings were at the operator's discretion. Three patients underwent an additional intervention (rotational atherectomy or cutting balloon) before excimer laser. Successful re-expansion, defined as an increase of at least 1 mm² in minimal stent cross-sectional area by intravascular ultrasound or a ≥20% increase in minimal stent diameter as measured by coronary angiography, was achieved in 27/28 (97.4%) of patients. Minimal stent diameter increased by 1.1±0.7 mm. There were no periprocedural deaths, one periprocedural MI, and two patients with transient ST elevations. One patient with pre-existing severe left ventricular dysfunction died suddenly during 6 month follow-up, and one required target vessel revascularization. Symptom status or function during follow-up were not reported.

Seven case reports¹⁶⁻²² described the successful application of excimer laser (ie, improvement on angiography or relief of symptoms) followed by angioplasty to

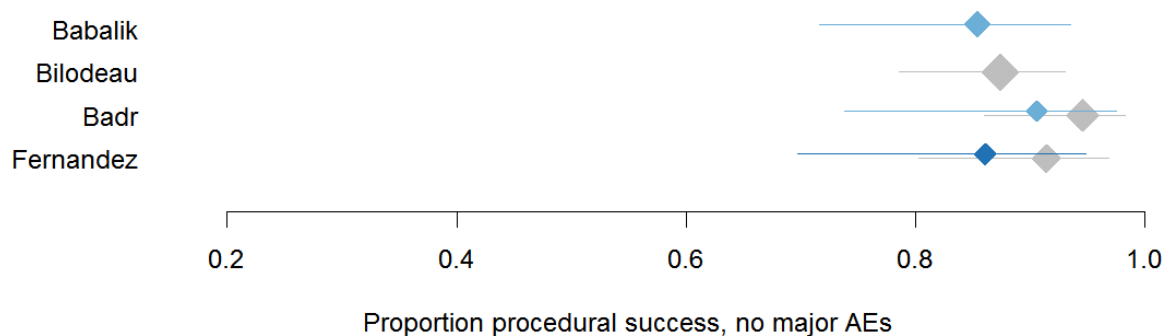
underexpanded stents. Patients were either treated as part of the initial interventional procedure (three patients), or after presentation with recurrent angina or acute coronary syndrome involving an underexpanded stent (three patients; one report could not be retrieved¹⁶). In three cases an ELCA1 0.9 mm high energy laser was used, and in three others an older generation 1.4 mm laser. Case reports described procedural success with symptom-free follow-up of up to 10 months. One report stated that there were no adverse events, and the remaining five did not report any.

Summary

Uncrossable lesions

Studies included 36 patients with balloon-uncrossable lesions and 244 patients with CTO, although results for the latter were in some cases reported in aggregate with other lesions. Rates of clinical success (which was generally defined as a successful procedure with no major adverse events occurring prior to discharge) was 86-91% (see Figure 1). There was one laser-related periprocedural fatality due to perforation, and in individual studies perforation rates ranged from not reported to 7%. Other periprocedural adverse events included coronary artery dissection, myocardial infarction, major bleeding, and ventricular fibrillation (Table 2).

Figure 1 Summary of procedural success without major AEs for studies of excimer laser atherectomy in patients with uncrossable lesions/ chronic total occlusions



Number and proportion of outcomes were as given in individual studies for a successful procedure without major adverse events, although the exact terminology varied. The symbol indicates a point estimate, the line the 95% confidence, calculated separately. Grey indicates results for all patients in a mixed series, light blue results for patients with CTO, dark blue results for patients with uncrossable lesions.

Under-expanded stents

Of 28 patients in one case series of patients with underexpanded stents, all but one had procedural success, with no deaths and one MI. In follow-up, one patient with pre-existing severe LV dysfunction died suddenly three months after the procedure; other long term outcomes outcomes were not reported.

Long-term follow-up and clinical outcomes

Apart from one case series reporting six-month follow-up in 48 patients, and a single mention of a death following discharge in another, there is no evidence reflecting the clinical consequences of this procedure.

Ongoing randomized controlled trials

Searches in ClinicalTrials.gov and Current Controlled Trials did not identify any relevant RCTs involving the use of excimer laser in these indications.

ELCA AT THE MUHC

ELCA has not previously been used at the MUHC; however it has previously been used by the local expert, Dr. Luc Bilodeau. The projected rate of use is approximately 10 patients per year.

Budget impact

In the absence of data about outcomes beyond the periprocedural term, we have calculated budget impact of the procedure alone. We considered only the cost of the catheters (ELCA Coronary Laser Atherectomy Catheter) as the laser generator itself is available without charge by previous arrangement between the MUHC and the manufacturer.

Each excimer laser is estimated to cost \$1500, and this is assumed to be an add-on cost to the currently used disposables. If the availability of an excimer laser enables a re-intervention, e.g., treatment of a patient with a symptomatic underexpanded stent, then the second PCI will cost approximately an additional \$6500 (based on 2007 costs for Ontario of a procedure without stent placement and without considering physician costs²³, local costs being unavailable). If the projected 10 patients were to undergo the procedure annually, the resulting additional cost to the MUHC would be between \$15,000 (assuming no additional procedures) and \$80,000 (assuming all additional procedures).

DISCUSSION

The literature reports a range of use of excimer laser for atherectomy/debulking of coronary lesions from clinical trials and registries, but reports in which it was used for the identified subsets of interest are limited to case series, registry studies and case reports. Furthermore, although the rates of procedural and clinical success were fairly high, the majority of these studies only described periprocedural outcomes.

On the assumption that there was likely to be substantial overlap between lesions considered balloon-uncrossable and the better studied subset of chronic total occlusions, we included reports of the use of excimer laser prior to stent implantation in chronic total occlusions. We recognize, however, that the two are not necessarily equivalent: balloon-uncrossable refers to the inability to pass a guidewire, without reference to perfusion or duration, while CTO is also defined by the duration of lack of flow across the lesion.

In the absence of chronic total occlusion, it is generally accepted that the relief of severe, symptomatic stenosis by angioplasty with stent placement will lead to long term benefit¹. High quality evidence for the long-term efficacy of angioplasty with stent placement in CTO is lacking; although successful intervention to reopen the artery appears associated with longer survival in retrospective observational studies and prospective registries^{8, 9, 24}. No RCTs or prospective observational studies directly compare intervention with best medical management in CTO^{8, 9, 24}. An HTA from the Ludwig Boltzman Institute (in German, therefore not included in our systematic review) on the use of excimer laser in CTO identified two observational studies^{6, 12} that were also included in the our evaluation, in addition to a single RCT using an older model of laser guidewire¹¹. The authors concluded that the evidence for excimer laser in CTO was insufficient to assess benefit and it was therefore not recommended,

Eine Aufnahme in den Leistungskatalog wird derzeit nicht empfohlen. Die vorhandene Evidenz ist nicht ausreichend, um den Netto-Nutzen der evaluierten Intervention beurteilen zu können²⁵.

The earlier literature on in-stent restenosis, e.g., that aggregated in the meta-analysis by Radke³, did not distinguish between patients with stenosis due to an underexpanded stent and stenosis due to new growth of the vessel lining. However, other authors attribute most if not all improvement on reintervention to ablation of new growth²⁶. The literature, describing outcomes for patients explicitly identified as having underexpanded stents is small, and the follow-up short.

CONCLUSIONS

- **The overall benefit of angioplasty with stent implantation is established, However failure may result in two small sub-groups of patients; those with uncrossable lesions and those with underexpanded stents.**
- **Evidence for the use of excimer laser atherectomy using current technology for these two indications is restricted to case series. Most of these report a fairly high rate of procedural success, but information on outcomes during follow-up is limited to one observational study (6 months).**

- **There is no evidence to support a conclusion that a successful procedure leads to symptomatic improvement or increased longevity.**
- **Reported serious adverse events are not infrequent. In a total of 261 procedures², one patient died as a result of perforation. Per-study rates of coronary artery dissection were 0-9.3%, myocardial infarction, 0-10.4%, and major bleeding, 0-6.2%.**
- **The additional cost to the hospital for 10 patients per year would be between \$15,000 (assuming no additional procedures) and \$80,000 (assuming all are additional procedures).**

RECOMMENDATIONS

The present evidence of benefit of this procedure is insufficient to justify the associated opportunity cost. It could be considered only as a fully funded research activity.

² These were not all uncrossable lesions or underexpanded stents, as some studies included several types of complex lesions and did not report results separately.

TABLES

Table 1 Studies using excimer laser atherectomy in patients with uncrossable lesions, chronic total occlusions and underexpanded stents: Study descriptions

| Author, Year | Design | Patients | Intervention | Endpoint | Other endpoints |
|---------------------------------|--|--|---|--|--|
| Uncrossable lesions | | | | | |
| Fernandez, 2013 ¹⁴ | Single centre (UK), retrospective case series. 2007-2011. | Patients with 'balloon failure' (failure to cross[FTC] or expand lesion) treated with ELCA±rotational atherectomy; stratified by CTO/non-CTO. | CVX-300 Excimer Laser System. Vitesse C 0.9 mm catheter. Saline flush technique. | Procedural success: stent deployment, residual stenosis <20% without major complication. | Complications: no-reflow, flow-limiting dissection, Q-wave MI, death. |
| Chronic total occlusions | | | | | |
| Badr, 2013 ¹³ | Single centre (US), retrospective case series 2004-2011 | Patients who underwent PCI with ELCA. Mixed case series including CTO n=32 | CVX-300 Excimer Laser system, 0.9-2.0 mm laser catheter. Flush-and-bathe technique. | Angiographic success: <50% residual stenosis after ELCA and adjunctive therapy. Clinical success: Procedural success w/o major clinical events at discharge. | Complications: Death, Q-wave MI, non-Q wave MI. Dissection type C or worse, coronary spasm, thrombus formation, no reflow, embolization, perforation, loss of major side branch, acute closure. |
| Bilodeau, 2004 ⁶ | Multicentre non-randomized comparative study of 2 laser protocols (Canada, Belgium, Netherlands) | Patients with single stenotic (or restenotic) lesion ≥80% with calcification by angiogram, or CTO. Excluded acute ischemic events, recent angioplasty, lesions uncrossable with guidewire. | CVX-300 Excimer Laser System. 0.9 mm X80 catheter at increased power and standard settings. | Procedural success: <50% residual stenosis after adjunctive therapy. Clinical: Procedural success without major adverse cardiac events by discharge. | Major adverse cardiac events: death, Q-wave MI, non-Q-wave MI, need for target lesion revascularization, tamponade. Ategrade flow by TIMI. Laser complications: dissection type C or worse, coronary spasm, thrombus formation, no reflow, embolization, perforation, loss major side branch, acute closure. |

| Author, Year | Design | Patients | Intervention | Endpoint | Other endpoints |
|-----------------------------|---|--|--|--|--|
| Uncrossable lesions | | | | | |
| Babalik, 2003 ¹² | Single centre (Turkey), retrospective case series. 1997-2000. | Patients with CTO and successful guidewire recanalization. Excluded: bend >60°, reference segment diameter <2 mm, excessive proximal tortuosity. | CVX-300 Excimer Laser System, 1.4-2.0 mm laser catheter. Saline infusions. | Procedural success: residual stenosis <50%, without major complication. Clinical success: residual stenosis <50%, survived hospitalization without MI, need for repeat angioplasty or bypass surgery. Event-free survival at 6 months. | Complications: death, bypass surgery, sustained coronary occlusion (TIMI 0), Q or non-Q wave MI. |
| Underexpanded stents | | | | | |
| Latib, 2014 ¹⁵ | Multicentre (UK), prospective observational (single-arm) | Underexpanded stent despite high pressure balloon inflation (de novo and ISR) | CVX-300 Excimer Laser system. Turbo elite catheter 0.9-2.0 mm. If optimal expansion not achieved, contrast injection used. | CSA increased $\geq 1 \text{ mm}^2$ or MSD $\geq 20\%$ | Procedural: vessel perforation, dissection, slow-flow or no reflow, MI. Follow-up: target lesion revascularization, MI, death, ST (per Academic Research Consortium) |

CSA, cross-sectional area; CTO, chronic total occlusion; ELCA, excimer laser coronary ablation; FTC, failure to cross; ISR, in-stent restenosis; LVEF, left ventricular ejection fraction; MI, myocardial infarction; mJ/mm², millijoules per square millimetre; MSD, minimal stent diameter; TIMI, Thrombolysis in Myocardial Infarction Grade Flow.

Table 2 Studies using excimer laser atherectomy in patients with uncrossable lesions, chronic total occlusion and underexpanded stents: Study results

| Author, Year | N | Age (years) | Male (%) | Results of procedure | Periprocedural AEs | Follow-up outcomes | Follow-up AEs |
|---------------------------------|-----------------------------|---------------|------------|---|--|---|--|
| Uncrossable lesions | | | | | | | |
| Fernandez, 2013 ¹⁴ | 58 (36 FTC) | 72±8.5 | 49 (84.1%) | Overall procedural success, 53 (91.3%). Success with ELCA alone, 43/58 (63.9%). Success for failure to cross lesions, 23/36 (63.9%). For failure to expand lesions, 20/22 (90.9%). Success with ELCA plus rotational atherectomy (RA), 31/36 (86.1%). | Periprocedural (all patients): Death, 1, following ELCA-associated Type III coronary perforation. Other AEs: Type I coronary perforation, 1. Transient no-reflow, no raised enzymes, 1. Transient occlusion side branch, 1. No flow-limiting coronary dissections. | Not reported | Not reported |
| Chronic total occlusions | | | | | | | |
| Badr, 2013 ¹³ | 119 (32 CTO) | 62±11.6 (CTO) | 23 (72%) | Angiographic success for CTO, 29/32 (90.6%). Clinical success for CTO, 29/32 (90.6%). | Dissection, 3. Major bleeding, 2. Perforation, 1. Thrombus formation, 1. CABG, 1. Intra-aortic pump emergent, 1. | Not reported | Not reported |
| Bilodeau, 2004 ⁶ | 95 (35 PCI failure, 28 CTO) | 67±11 | 68 (72%) | CTO not reported separately. Overall procedural success, 87/95 (92%). Clinical success, 83/95 (86%). | AEs (all patients). Dissection, 5. Periprocedural vfib requiring resuscitation, followed by MI, 1. | Not reported | Not reported |
| Babalik, 2003 ¹² | 48 | 55±10.1 | 44 (92%) | Procedural success, 46 (95.8%). Clinical success, 41 (85.4%) | Q-wave MI, 1. Non-Q wave MI, 4. | 6-month (n=46): Event-free survival 35 (76%). Angiographic restenosis 20 (44%), | Repeat angioplasty 9 (19.5%), bypass operation 1 |

angiographic
reocclusion 7 (15%) (2.1%)

Underexpanded stents

| | | | | | | | |
|---------------------------|---------------------------|-----------|--------------|---|--|--------------|---|
| Latib, 2014 ¹⁵ | 28 (25 ISR, 3 de novo) | 71.5±10.5 | 19 (67.9) | Success, 27 (96.4%). MSD increased 1.1±0.7 mm, MSA increased 3.6 mm ² (17 patients) | Periprocedural AEs: MI, 1. Transient ST elevation, 2. | Not reported | 6-months follow-up: cardiac death 1 (sudden death in patient with severe LV dysfunction) at 3 months. |
|---------------------------|---------------------------|-----------|--------------|---|--|--------------|---|

CABG, coronary artery bypass graft; CSA, cross-sectional area; CTO, chronic total occlusion; ELCA, excimer laser coronary ablation; FTC, failure to cross; FTE, failure to expand; ISR, in-stent restenosis; LV, left ventricle; LVEF, left ventricular ejection fraction; MI, myocardial infarction; mJ/mm², milliJoules per square millimetre; MSA, minimal stent area; MSD, minimal stent diameter; TIMI, Thrombolysis in Myocardial Infarction Grade Flow.

REFERENCES

1. Levine GN, Bates ER, Blankenship JC, Bailey SR, Bittl JA, Cercek B, et al. 2011 ACCF/AHA/SCAI Guideline for Percutaneous Coronary Intervention. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. *J Am Coll Cardiol*. 2011;58:e44-122.
2. Bittl JA, Chew DP, Topol EJ, Kong DF, Califf RM. Meta-analysis of randomized trials of percutaneous transluminal coronary angioplasty versus atherectomy, cutting balloon atherotomy, or laser angioplasty. *J Am Coll Cardiol*. 2004;43:936-42.
3. Radke PW, Kaiser A, Frost C, Sigwart U. Outcome after treatment of coronary in-stent restenosis: Results from a systematic review using meta-analysis techniques. *European Heart Journal*. 2003;24:266-73.
4. Spectranetics. ELCA coronary laser atherectomy catheter: Spectranetics; 2014 [March 27, 2014]. Available from: <http://www.spectranetics.com/physicians/coronary-vascular-intervention/products/ecla-coronary-laser-ablation/>.
5. Spectranetics. Turbo Elite laser atherectomy catheter: Spectranetics; 2014. Available from: <http://www.spectranetics.com/physicians/peripheral-vascular-intervention/products/turbo-elite/>.
6. Bilodeau L, Fretz EB, Taeymans Y, Koolen J, Taylor K, Hilton DJ. Novel use of a high-energy excimer laser catheter for calcified and complex coronary artery lesions. *Catheter Cardiovasc Interv*. 2004;62:155-61.
7. Blicq EG, Jean-Louis, Gibault-Genty G, Aziza J-P, Jemaa KB, Jerbi B, Livarek B. Therapeutic impact of the stent visualization enhancement technique (StentBoost(R)) in percutaneous coronary intervention. *Arch Cardiovasc Dis*. 2012;4:5.
8. Sianos G, Werner GS, Galassi AR, Papafaklis MI, Escaned J, Hildick-Smith D, et al. Recanalisation of chronic total coronary occlusions: 2012 consensus document from the EuroCTO club. *EuroIntervention*. 2012;8:139-45.
9. Interventional procedure overview of percutaneous laser coronary angioplasty. UK: National Institute for Health and Clinical Excellence, 2010. Available from: <http://www.nice.org.uk/nicemedia/live/12804/50606/50606.pdf>
10. Interventional procedure guidance: Percutaneous laser coronary angioplasty. UK: National Institute for Health and Clinical Excellence, 2011. Available from: <http://www.nice.org.uk/nicemedia/live/12804/52632/52632.pdf>
11. Serruys PW, Hamburger JN, Koolen JJ, Fajadet J, Haude M, Klues H, et al. Total occlusion trial with angioplasty by using laser guidewire. The TOTAL trial. *Eur Heart J*. 2000;21:1797-805.
12. Babalik E, Gurmen T, Gulbaran M, Ersanli M, Ozturk S. Revascularization of chronic coronary artery occlusions using laser debulking followed by stent implantation. *Acta Cardiol*. 2003;58:149-53.
13. Badr S, Ben-Dor I, Dvir D, Barbash IM, Kitabata H, Minha S, et al. The state of the excimer laser for coronary intervention in the drug-eluting stent era. *Cardiovasc Revasc Med*. 2013;14:93-8.
14. Fernandez JP, Hobson AR, McKenzie D, Shah N, Sinha MK, Wells TA, et al. Beyond the balloon: Excimer coronary laser atherectomy used alone or in combination with rotational atherectomy in the treatment of chronic total occlusions,

- non-crossable and non-expandable coronary lesions. *EuroIntervention*. 2013;9:243-50.
15. Latib A, Takagi K, Chizzola G, Tobis J, Ambrosini V, Niccoli G, et al. Excimer Laser LEsion Modification to Expand Non-dilatable sTents: The ELLEMENT Registry. *Cardiovasc Revasc Med*. 2014;15:8-12.
 16. Goldberg SL, Colombo A, Akiyama T. Stent Under-Expansion Refractory to Balloon Dilatation: A Novel Solution with Excimer Laser. *J Invasive Cardiol*. 1998;10:269-73.
 17. Sunew J, Chandwaney RH, Stein DW, Meyers S, Davidson CJ. Excimer laser facilitated percutaneous coronary intervention of a nondilatable coronary stent. *Catheter Cardiovasc Interv*. 2001;53:513-7; discussion 8.
 18. Noble S, Bilodeau L. High energy excimer laser to treat coronary in-stent restenosis in an underexpanded stent. *Catheter Cardiovasc Interv*. 2008;71:803-7.
 19. Viceconte N, Biscione C, Tarsia G, Osanna R, Polosa D, Del Prete A, et al. Laser "explosion" technique for treatment of unexpanded coronary stent. *Int J Cardiol*. 2011;149:395-7.
 20. Egre M. A novel approach for under-expanded stent: Excimer laser in contrast medium. *Journal of Invasive Cardiology*. 2012;24:E161-E3.
 21. Lam SC, Bertog S, Sievert H. Excimer laser in management of underexpansion of a newly deployed coronary stent. *Catheter Cardiovasc Interv*. 2014;83:E64-8.
 22. Ben-Dor I, Maluenda G, Pichard AD, Satler LF, Gallino R, Lindsay J, et al. The use of excimer laser for complex coronary artery lesions. *Cardiovasc Revasc Med*. 2011;12:69 e1-8.
 23. Bowen JM, Hopkins R, Chiu M, Blackhouse G, Lazzam C, Ko D, et al. Clinical and cost effectiveness analysis of drug eluting stents compared to bare metal stents for percutaneous coronary interventions in Ontario. Hamilton, ON, Canada: Program for Assessment of Technology in Health (PATH), St. Joseph's Healthcare Hamilton / McMaster University, 2007.
 24. Tamburino C, Capranzano P, Capodanno D, Dangas G, Zimarino M, Bass TA, et al. Percutaneous recanalization of chronic total occlusions: wherein lies the body of proof? *Am Heart J*. 2013;165:133-42.
 25. Johansson T, Mathis S. Laser angioplasty of coronary arteries. Vienna, Austria: Ludwig Boltzmann Institut für Health Technology Assessment, 2010. [Accessed 2014/01/30/18:51:39]. Available from: http://eprints.hta.lbg.ac.at/885/1/DSD_39.pdf
 26. Mehran R, Mintz GS, Satler LF, Pichard AD, Kent KM, Bucher TA, et al. Treatment of in-stent restenosis with excimer laser coronary angioplasty: mechanisms and results compared with PTCA alone. *Circulation*. 1997;96:2183-9.