regenerate

SLT FROM ELLEX

VOL 11 | NOVEMBER 2009

IN THIS ISSUE

Highlights

"SLT has become part of the standard of care for the treatment of glaucoma patients in France. More than 100 clinical centers are now equipped with SLT technology, and at the Edouard Herriot Hospital, we have successfully performed hundreds of SLT treatments." **See page 2.**

Philippe Denis, MD, PhD, France.

Long-Term Experience with SLT

Ellex SLT Symposium at the ESCRS 2009

For the fourth year, Ellex hosted an SLT lunch symposium at the European Society of Cataract and Refractive Surgeons (ESCRS) meeting, held in Barcelona. The overflow of more than 180 physicians from around the globe confirmed that selective laser trabeculoplasty (SLT) is now seen as a key component of glaucoma therapy.

The Ellex SLT symposium, which was part of the EuroTimes Satellite Education Program, was chaired by Professor Julian Garcia Feijoo from San Carlos Clinical Hospital, Madrid. The faculty included a well-known panel of international experts, including Lawrence F. Jindra, Columbia University; Peter Kaulen from Berlin; Jose Maria Martinez de la Casa from Madrid; and Madhu Nagar from Wakefield, U.K.

Besides a special focus on long-term results for both primary and repeat treatments, the presentations touched on the place of SLT in glaucoma management, its risk-benefit ratio, its cost effectiveness, and how various treatments compare to each other.

The Limits of Medical Treatment

Professor Garcia Feijoo opened the symposium by assessing the current challenges of glaucoma management and reminding the audience that glaucoma

continued, page 6

Economy Shifts Focus to SLT

The global financial landscape has changed significantly in recent times. A wide-sweeping credit meltdown and plummeting world trade caused havoc, pushing many of the world's leading economies into recession. But signs of a recovery have recently emerged. Economic growth has tentatively resumed in many key markets, but unlike the rapidly spreading and powerful financial crisis, the recovery appears to be slow and fragile.

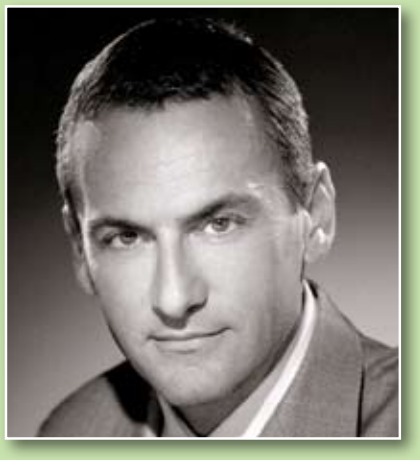
Given such realities, it is no surprise that many in the eye care world are giving selective laser trabeculoplasty (SLT) a closer look. The surgery is easy to learn and perform, lowers IOP as effectively as drug therapy, has a consistent safety profile and—best of all—can with one simple, in-office procedure drastically reduce glaucoma patients' reliance on years of treatment with expensive medications.

continued, page 8

SLT Clinical Tips

Philippe Denis, MD, PhD, University Hospital of Lyon, France

SLT has become part of the standard of care for the treatment of glaucoma patients in France. More than 100 clinical centers are now equipped with SLT technology, and at the Edouard Herriot Hospital, we have successfully performed hundreds of SLT treatments. As a non-invasive procedure that is free of thermal effects to the trabecular meshwork (as opposed to ALT), SLT has an excellent safety profile and has now become the therapy of choice in the management of primary open-angle glaucoma. Because the energy and exposure time of SLT treatment are much lower than ALT and create no harm to the trabecular meshwork (TM), repeat treatments show excellent results without compromising the outcome of future surgery, if it is required.

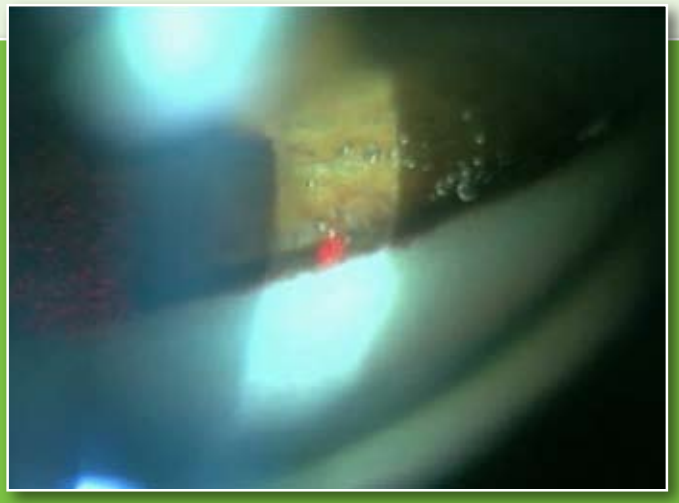


SLT Results

An average drop in intraocular pressure from 20 to 30 percent[1-3] can be expected following SLT treatment, which positions SLT favorably when compared with a medical monotherapy. It is worth mentioning that during the days following laser treatment, IOP often shows a significant decrease that is most likely due to the inflammatory reaction induced by the treatment. I recommend waiting at least one month before determining the success of the procedure, as some patients may be late responders to SLT.

Long-term Efficacy of SLT

Selective trabeculoplasty remains efficacious over the long term, with an average IOP decrease of 20 percent five years after treatment[1-3]. In several studies, the efficacy of SLT slowly decreases over time; approximately 10 percent of patients every year will fall below the 20 percent IOP reduction threshold. If IOP reduction has been effective over several years following initial SLT treatment, then I recommend repeating the SLT treatment as required, because repeat SLT has been shown to be as successful as initial SLT, with a similar IOP reduction as initial treatment[4].



Professor Philippe Denis has recently released an educational DVD on SLT, providing both current and future SLT practitioners with a comprehensive clinical and practical overview of SLT for glaucoma management. This DVD (currently available in French language only) is available on request from Ellex via slt@ellex.com.

Videos of live SLT treatment for a number of clinical cases featured on the DVD can also be viewed on the Ellex SLT website at slt-ellex.com.

References

1. Gracner et al. Long-term follow-up of SLT in primary open-angle glaucoma, Klin Monatsbl Augenheilkd ; 223:743-7, 2006.
2. Weinland et al. Long-term clinical results of selective laser trabeculoplasty in the treatment of primary open angle glaucoma, Eur J Ophthalmol 16:100-4, 2006.
3. Jindra et al. Selective Laser Trabeculoplasty: Clinical Perspective, ACES 2009
4. Hong et al. Repeat selective laser trabeculoplasty, J. Glaucoma 18:180-3, 2009.

Clinical Tips for Selective Laser Trabeculoplasty

- A narrow angle does not necessarily mean that SLT treatment is not indicated. SLT can be performed as long as the trabeculum can be observed during gonioscopy. When the angle is narrow but open, I usually prescribe pilocarpine to open the angle, thereby allowing me to perform SLT treatment more easily.
- The choice of the gonioscopy lens is crucial, as the optical magnification helps me to determine the spot size and the energy I need to deliver to the trabecular meshwork.
- To perform SLT, I always ensure that my patient is comfortably seated in front of the slit lamp. The gonioscopy lens needs to be positioned perpendicular to the eye axis. In order to visualize the trabecular meshwork in cases of iris bombe, do not move the lens, but instead ask the patient to look towards the lens mirror.
- When performing SLT, I recommend treating the trabecular meshwork over 180-degrees, starting from the inferior area of the angle (from 3 to 9 o'clock) or from its temporal area. Place 50 consecutive but not overlapping spots. It is important to note that the inferior and temporal areas of the TM are usually larger than the superior or nasal areas, which enhances the visibility of the structures and thereby makes the treatment easier. Should an enhancement treatment be required to further reduce IOP, treat the other 180-degrees at least one month following the initial SLT treatment.
- SLT is not indicated for congenital and juvenile glaucoma – in these cases, filtrating surgery should be performed.
- To avoid any post-laser inflammatory reaction of the anterior chamber, I usually prescribe non-steroidal anti-inflammatory drops for a few days. I also usually prescribe an alpha-2 adrenergic agonist before the SLT treatment to avoid post-treatment ocular hypertension.
- I always wait for a few weeks before assessing the IOP-lowering efficacy of SLT treatment: not all patients respond immediately, and there may be some "late responders." During this timeframe, I continue to treat patients with their previous medications.
- I strongly believe in the efficacy of repeat treatment with SLT. I usually wait at least six months before performing repeat treatment, always following the same protocol. Repeat treatment is, however, useless for patients who were not responders to initial SLT treatment.

Efficacy of Selective Laser Trabeculoplasty, with Special Attention to Health-Economic Aspects

Jürgen Reese M.D., Mark Tomalla M.D., Duisburg, Germany

Regenerate recently spoke with leading SLT users Jürgen Reese M.D and Mark Tomalla M.D regarding the role of SLT in glaucoma management. Both physicians have considerable experience with SLT, and are currently undertaking an open, non-controlled prospective study to investigate the efficacy of SLT. In particular, the study will address the following:

- The efficacy of SLT in patients undergoing drug therapy with one to three different glaucoma medications (eye drops), whose intraocular pressure cannot be adequately reduced.
- The possibility of longer- or long-term eye drop reduction after SLT, which also addresses the health-economic aspects of SLT.

We recently shared our preliminary, three-month results during the scientific program at the DOC 09 (22nd International Congress of German Ophthalmosurgeons) in Nuremberg, Germany. Thus far, 65 patients meeting the following inclusion criteria have been enrolled in the study:

- **Patients with pOAG (including NTG), PEX and pigment dispersion glaucoma**
- **Patients receiving drug treatment with one to three different glaucoma eye drops**
- **Patients whose target pressure could not be achieved**

In addition, the usual exclusion criteria applied and patients with the following were excluded from the study:

- **Narrow angle and closed angle glaucoma**
- **Previous intraocular procedures and fistulating operation**
- **Juvenile and congenital glaucoma**
- **Malformation blocking the chamber angle**
- **Missing view into the chamber angle**

According to our study protocol and to avoid a paradox IOP rise, we did not administer additional medications pre-operatively. Post-operatively, we did not administer any additional anti-inflammatory drops. All study participants undergo strict weekly controls the first month after SLT treatment.

Following SLT, the patients could be assigned to three groups:

1. Treatment with eye drops was withdrawn in 41 patients
2. Drug therapy was reduced in another six patients
3. Therapy with eye drops had to be continued, unchanged, in 18 patients

No serious complications occurred during or after the SLT treatment. In isolated cases, there was a slight conjunctival injection, as well as a slight anterior chamber cell finding that abated spontaneously. There was a transient paradox IOP increase in two patients.

At three months follow up, we observed that 75 percent of the patients achieved a consistent mean IOP reduction of approximately 20-25 percent, despite withdrawal or reduction of medication. In the remaining 25 percent of patients, there was no SLT treatment effect.

From a health-economic point of view, the costs to undergo SLT treatment at 298,04 euros roughly equates to the annual costs of undergoing medical treatment using Xalatan®, at 297,56 euros*. SLT makes sense from a health-economic point of view, especially in elderly glaucoma patients who must be treated with several preparations or combination preparations.

We can draw the following conclusions based on our experience to date:

- SLT is an effective, non-thermal laser procedure for the treatment of even extensively, unsuccessfully treated glaucoma patients.
- The procedure can be repeated and can be performed without serious side effects or complications.
- The use of SLT is also sensible from a health-economic point of view.

Our study results indicate that SLT is definitely plausible as primary or secondary glaucoma therapy, which is supported, among other things, by the markedly improved compliance that is achieved.

SLT or ALT	298,04
Monotherapy	
Vistagan 0,5%	77,08
Timo EDO 0,5%	88,65
Timo Comod	118,32
Brimodin Hexal	205,48
Azopt	235,80
Trusopt S	270,18
Alphagan	279,92
Lumigan	284,16
Xalatan	297,56
Combination Therapy	
Combigan	287,04
SLT or ALT	298,04
Ganfort	308,72
Cosopt	310,80
Cosopt S	314,22
Xalacom	329,48
Xalatan+Cosopt	608,36

* Official selling prices Germany, May 2009.

Editor's Note:
Regenerate would like to congratulate Dr. Tomalla and Dr. Reese on these initial clinical findings, and look forward to seeing the long-term results of their study. Based on these findings, it appears that SLT is an efficacious solution for patients with pOAG, PEX and pigment dispersion glaucoma, and offers a cost effective solution with many health-economic benefits.

Prediction Rule Analysis Demonstrates Efficacy of SLT with Prostaglandins

Cindy Hutnik, MD, PhD, FRCSC, University of Western Ontario, Canada


Cindy Hutnik

Although never shown in well-controlled studies, there have been suggestions that SLT is less efficacious when paired with topical prostaglandin anti-glaucoma medications. This is a significant clinical question since prostaglandin analogues are accepted as first line medical therapy and SLT is often used as an adjunctive glaucoma treatment. The purpose of this retrospective observational prediction rule analysis study was to determine if any of the major classes of anti-glaucoma therapies are positively or negatively associated with SLT success.

Testing SLT in Conjunction with Anti-Glaucoma Eye drops

To be eligible for the study, patients with an IOP of > 22 mmHg despite being treated with various multiple classes of anti-glaucoma medications were considered. The study examined 262 eyes of patients with primary open angle glaucoma (POAG), secondary OAG with pseudoexfoliation or pigment dispersion, normal tension glaucoma or ocular hypertension. Treatment success was defined as ≥ 20 percent IOP reduction from baseline at 6 months following SLT therapy. We hypothesized that SLT efficacy is diminished when used in conjunction with prostaglandin analogues but is enhanced in conjunction with carbonic anhydrase inhibitors.

After exclusion of eyes based on inadequate follow-up, 203 eyes were analyzed. The univariate analysis indicated that SLT success was enhanced in conjunction with a fixed combination of timolol and dorzolamide, the latter being a carbonic anhydrase inhibitor. A multivariate logistic regression analysis was then performed to determine if this, and other parameters held up as SLT success predictors.

Only two pre-SLT parameters were identified in the rigor of the multivariate analysis as predictors. A positive predictor of success (odds ratio of 1.320) was the IOP elevation just prior to SLT treatment (within 4 weeks). A negative predictor of success (odds ratio 0.914) was the maximum IOP ever recorded. Overall, 64.53 percent of eyes experienced an IOP reduction of > 20 percent at 6 months post SLT.

These prediction analyses showed that topical medications did not adversely or favorably affect SLT success. Anterior chamber angle pigmentation, diabetes, gender, corneal thickness, pseudophakia, specific glaucoma diagnosis, eye drop washout and previous ALT treatment were also not associated with SLT treatment success.

SLT: A Success as Primary or Adjunct Therapy

In an analogous manner to prostaglandin medical monotherapy, SLT works best in an eye with high IOP just prior to treatment. If a prostaglandin is added to an eye already on 4 other eye drops, it doesn't work as effectively. I equate SLT to an ideal eye drop with demonstrated safety and efficacy. SLT sometimes gets a 'bad rap' because it is often used later in the treatment paradigm, similar to ALT. SLT is no different from an eye drop in that it works best in a treatment naïve eye. It is a useful adjunct to medical therapy early in the treatment paradigm and has great utility later in situations where a reduction in the dependency of medical therapy is required owing to intolerable side effects, compliance issues and/or cost to the healthcare system.

Cost-effectiveness and Compliance

We published data in the Canadian Journal of Ophthalmology, which showed the cost-effectiveness of SLT. Patients with high IOPs were treated with different classes of IOP lowering medications. On average, pretreatment IOP was above 24 mmHg and post treatment IOP was 16 mmHg. Patients were then treated with SLT to determine if eye drop dependency could be reduced. Following SLT therapy, pressures reduced to 13 mmHg. As patients were on 3-4 different topical medications prior to SLT, the 3 mmHg reduction was welcomed. SLT thus functions as a very effective 'preservative-free' option for these patients, sustaining a low IOP, reducing cost burden, routine of multiple bottles, potential washout effect of using several drops simultaneously, as well as improving the ocular surface by reducing the load of chemicals that contributed to ocular surface disease.

I've used SLT for over eight years and recommend it as both a primary and adjunctive therapy. While I recommend monotherapy prostaglandin as first line treatment, if patients do not reach target pressure, I often recommend SLT as the second choice adjunctive therapy. I also do not hesitate to recommend SLT as a first line therapy in certain patients.

Based upon this prediction rule analysis it is enticing to consider a future multi-center, prospective clinical study that further explores the intriguing suggestion that some topical medications may enhance SLT efficacy. In conclusion, this current study demonstrates that prostaglandins do not interfere with SLT therapy outcomes.

remains the leading cause of irreversible blindness in Western countries. He then explained that the three main objectives of every glaucoma treatment should be to stop disease progression, have as little impact as possible on the patient's quality of life and represent reasonable costs for both the patient and health organizations.

Because medications are used as first-line treatment in many countries, he analyzed their limitations in light of these three criteria. "Patients tend to forget or have difficulty instilling medications, miss some doses or often take them at the incorrect time," Professor Garcia Feijoo explained. "Further limitations of medications include adverse events, compliance issues, treatment cost, and the impact on quality of life."

As a transition to the presentations from the panel, he addressed the question of whether SLT, as opposed to medical treatment, can be summarized as "fire and forget" (F&F). In the ensuing presentations, the panel addressed whether SLT as a primary and repeat treatment is efficacious on the long-term, and if it can indeed be considered as F&F.

Seven-Year Results with SLT as Repeat Treatment

In his presentation, Dr. Jindra examined the cumulative incidence of repeat therapy with SLT for patients with glaucoma. For this purpose, a retrospective chart review was performed on 2,419 eyes from a consecutive case series of 3,048 eyes over seven years. Eyes were divided into those treated with primary and secondary therapy; into subgroups of 0-2, 2-4, and 4-6 years of follow-up; and then were randomly selected for analysis. The rates of repeat and times until repeat were analyzed.

In this series over the long term, repeat rates after primary SLT at all time intervals examined were significantly less than repeat rates after secondary SLT (Figure 1), and time to repeat after primary SLT at all time intervals examined was significantly more than time to repeat after secondary SLT (Figure 2).

Years of Follow-Up	Primary Patients Repeat Rates (%)	Secondary Patients Repeat Rates (%)
0-2	5	40
2-4	10	60
4-6	9	46

Figure 1: Comparative chart of repeat rates for eyes which had SLT as primary or secondary treatment

Years of Follow-Up	Primary Patients Time to Repeat (Days)	Secondary Patients Time to Repeat (Days)
0-2	325	298
2-4	1005	901
4-6	1837	1619

Figure 2: Comparative chart of time to repeat treatment for eyes which had SLT as primary or secondary treatment

In this series, 588 eyes out of 2,419 eyes initially treated with SLT required repeat treatment. Dr. Jindra concluded that in this series, repeat treatment with selective laser trabeculoplasty significantly lowered intraocular pressure, significantly lowered the number of medications and demonstrated a clinically effective repeat rate.

Twelve-Year Results with SLT

For the first time in the history of SLT, 12-year results were presented during an international meeting. Dr. Kaulen, a pioneer in the use of SLT as a primary therapy option, presented his follow-up results of more than 2,000 eyes treated with this laser therapy. In his symposium presentation, Dr. Kaulen shared the results of his prospective follow-up study involving 502 eyes of 330 patients. The mean follow-up time was 33 months, ranging from 1 to 144 months.

The results from his study showed that SLT is effective for POAG, PEX, ocular hypertension, and pigmentary glaucoma with success rates of 90 to 70 percent after three years, 60 to 75 percent after five years and 40 to 60 percent after 10 years. He specified that the success rate is, however, dependent on the indication (figure 3).

Based on his findings and on his very long-term experience with SLT, Dr. Kaulen concluded that selective laser trabeculoplasty provides good long-term results for POAG, ocular hypertension, PEX and pigmentary glaucoma, offers acceptable long-term results with eyes previously treated with ALT or SLT, and is of course repeatable.

The Spanish Experience with SLT

The experience with SLT in Spain was the central theme of Dr. Martinez de la Casa's presentation. Based on the results from

a study conducted by Dr. Martinez de la Casa et al. comparing SLT with conventional ALT, this presentation addressed hypotensive efficacy, anterior chamber inflammation and pain reported by the patients treated. In this prospective study performed on 40 consecutive patients over a six-month follow-up, no statistical difference between ALT and SLT groups was found with regards to changes in IOP during follow-up; however, flare was found to be statistically lower in the SLT group one hour after treatment. In addition, pain reported by patients during treatment was also lower in the SLT group.

Based on these findings and on the results from other studies he presented during this SLT session, Dr. Martinez de la Casa concluded that SLT is increasingly used in Spain to lower IOP.

"SLT is an effective procedure that achieves short- and long-term results similar to ALT," he said. Selective laser trabeculoplasty, however, has a milder effect in the trabecular meshwork, is very safe with only minor side effects and allows re-treatments. SLT is also technically easier to perform than ALT due to the larger spot size. It should however be used with caution in heavily pigmented angles."

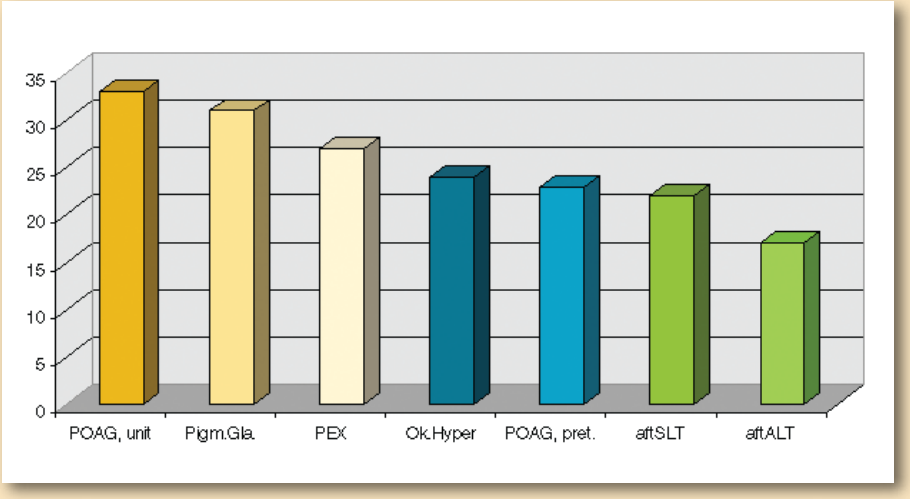


Figure 3: IOP reduction (in %) for different indications over a mean follow-up of 3 years post-SLT treatment

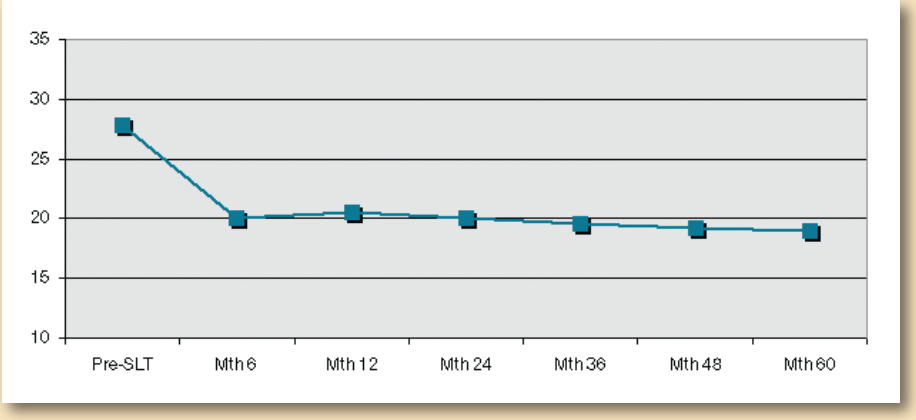


Figure 4: Primary SLT and IOP drop for OAG and OHT (follow-up of 54 months)

Long-Term Results with SLT as First-Line Therapy

Closing out the symposium, Madhu Nagar presented results from a case study analysis of SLT procedures in which 778 eyes of 452 patients were analyzed. Out of these, 53 percent received SLT as primary treatment, while the remaining 47 percent received it as an adjunctive or replacement therapy.

In the primary group, IOP fell from 27.8 mmHg to 19 mmHg after a follow-up period of 54 months, which represents a 32 percent reduction in IOP (Figure 4).

In the secondary group, a 33 percent reduction in IOP was recorded after 59 months. Nagar's conclusion from these results was that SLT has positive long-term prospects and is a repeatable treatment. Madhu Nagar also believes that selective laser trabeculoplasty can be used as first line, adjunctive and replacement therapy and should be considered as therapy of choice in the glaucoma treatment paradigm.

Her current profile for patients who already are on medical therapy and/or under maximally tolerated medical therapy is to wash medical treatment completely or partly before selective laser trabeculoplasty, restart medical therapy if required if insufficient IOP reduction is achieved following laser treatment, and eventually perform surgical filtering if both SLT and medications fail to control IOP.

"For me, SLT is now number one", she concluded. "No other method has a better risk-benefit ratio than selective laser trabeculoplasty."

continued, page 8

Long-Term Experience with SLT, continued from page 7

Questions From the Audience to the Panel of Experts

The following interactive session showed that everyone has a slightly different way of performing SLT, which led Dr. Jindra to conclude the session by stating, "SLT seems to know what to do without us telling SLT what to do."

Question: "Do you spare any quadrant of the trabecular meshwork for some future filtering surgery in case anything goes wrong?"

Lawrence F. Jindra: "I do spare the top 4 clock hours – but for no good reason I must say, other than habit, as SLT has not been shown to impact on the outcome of future surgery".

Question: "Do you prescribe any medications before SLT treatment?"

Jose Maria Martinez de la Casa: "I usually prescribe brimonidine before the laser treatment and during the day following treatment."

Madhu Nagar: "I personally prescribe one drop prior and one drop after laser."

Question: "Should some anti-inflammatory drops be prescribed following SLT treatment?"

Lawrence F. Jindra: "Although they are not needed, I do prescribe some for the sake of my patients' comfort."

Madhu Nagar: "The anterior chamber inflammation induced by SLT is natural and if it is left as is, it will disappear by itself."

Question to Madhu Nagar: "I know you wash out medications before SLT. How do you proceed?"

Madhu Nagar: "I usually start by washing off the drop that the patient took the longest. I have left all my patients on prostaglandins as compliance is better with once a day dosage and try and wash off every other medication. I do also spend some time with my patients before washing-off treatment to understand their routine, issues with any with treatment regimen and then agree on a treatment plan with them."

A webinar of the Ellex SLT symposium at ESCRS, including the interactive panel session, will soon be available on slt-ellex.com.

Upcoming Events

VII Russian Glaucoma Society Annual Meeting

- SLT Presentation by Prof. Shlomo Melamed
- 4 December 2009
- Moscow, Russia

SLT Symposium: "SLT - Results from Kuwait"

- 9 December 2009
- Salmiya, Kuwait

Register via slt@ellex.com

Economy Shifts Focus to SLT, continued from page 1

An editorial published in the May 2009 edition of Ophthalmology put into words the feelings of a growing number of practitioners.[1] After reviewing current literature regarding the cost-effectiveness of glaucoma treatment algorithms, it concluded that moving SLT to the front of first-line glaucoma therapy, while retaining drug therapy as a second-line option, increased efficacy and saved large sums of money.

"A change to initial laser trabeculoplasty followed by topical medication and then trabulectomy was surprisingly cost-effective and was actually a cost savings, returning $2.50 for every $1.00 spent," the article said. "Even if the cost of laser treatment increased four-fold, it still returned $1.74 for each $1.00 spent."

The editorial goes on to take what appears to be a jab at the pharmaceutical industry and its researchers for failing to give sufficient clinical attention to SLT as viable treatment option: "One can only guess at the impact that the lack of well funded champions to promote laser trabeculoplasty over available pharmaceutical products may have had on our prescribing habits and the costs of managing glaucoma."

In addition to its favorable profile from a health economics perspective, SLT as a first-line therapy would all but eliminate worries over patient drug therapy compliance, which recent studies have proven to be deficient. "[M]uch more consideration should be given to laser trabeculoplasty as the initial treatment. It should be considered as 'a first drop,' and additional medications introduced as needed," the editorial concluded.

Reference:
Taylor HR. Glaucoma: Where to Now? Ophthalmology. May, 2009. 116(5):822.

For more information visit
slt-ellex.com

ellex

ellex.com

Headquarters
82 Gilbert Street
Adelaide, SA, 5000 AUSTRALIA
+61 8 8104 5200

Japan
4-3-7 Miyahara 4F, Yodogawa-ku
Osaka 532-0003 JAPAN
+81 6 6396 2250

USA
7138 Shady Oak Road
Minneapolis, MN, 55344 USA
1 800 824 7444

Europe Support Center
108, avenue Marx Dormoy
63000 Clermont-Ferrand FRANCE
+33 4 73 34 18 55