Interview to Professor Christer Lindquist

Neurosurgeon, Bupa Cromwell Hospital, Cromwell Road, LONDON

Professor Lindquist, why Neurosurgery?

Serendipity. I liked physiology during the second year of medical school and started working in the physiology department, eventually writing my PhD thesis in neurophysiology. I also enjoyed the surgical course. From there it was a small step to neurosurgery.

Who were your teachers when you started Neurosurgery?

My very first year in neurosurgery was as a resident under Prof. Robert Grossman at the University of Texas Medical School in Galveston. Through him I came to know Dr Steiner at the Karolinska in Sweden. Dr Steiner invited me for an interview and I continued my neurosurgical residency at the Karolinska in Sweden 1976. I soon got involved in research projects with then retired Prof. Lars Leksell. He also started his research career in neurophysiology and he was a great inspiration for me.

Did you immediately get involved in the field radiosurgery?

No. In fact, I was more interested in microsurgery. Prof. Ladislau Steiner was the champion of microsurgery at the Karolinska. I was fortunate to be one of his disciples. His mentor- and friend-ship continued until he passed away at the age of 92. His subspecialty was vascular microsurgery and all patients with aneurysms and arteriovenous malformations were treated under his leadership, which I took over after his retirement. Arteriovenous malformations are arguably the most difficult lesions to treat by microsurgery and it was a leap forward when Steiner and Leksell in 1970 were able to

successfully treat the first case by Gamma Knife Surgery. Radiosurgery therefore became an integral part of the treatment armamentarium for AVM, but also for skull base tumours. I was intrigued by the good outcomes and therefore became more and more involved.

Was there any equipment that you helped to develop in those early years?

Yes – helped, with the emphasis on helped. Leksell was continuously refining his stereotactic instruments. Steiner and I were involved in developing the model G of Leksell's stereotactic frame, which is currently used in SRS as well as for invasive stereotactic procedures. Invasive procedures included image guided craniotomies. For craniotomies Steiner and I developed the "Steiner-Lindquist" microsurgical guide. The guide is a laser beam on a holder, which is attached to the stereotactic G-frame with coordinates based on preoperatively obtained stereotactic MR- or CT-images, which make the laser beam always showing the pathway towards the pathology to be resected.

Was there a lot of collaboration or did you treat SRS cases on your own?

Of course, I treated most of my patients on my own, but there was always indispensable collaboration especially with neuroradiologists but also physicists. Notably, the radiation oncologists at the Karolinska showed a very low interest in radiosurgery during the first 2 decades.

Any particular successes spring to mind?

The most striking success, which started the whole enthusiasm for radiosurgery in our microvascular team was the first obliteration of an AVM after doing a so-called "gamma ligature". The target was the large feeding arteries (nicknamed "Gamma ligature") and not the nidus. It was probably just a coincidence or (again) serendipity that the patient's AVM occluded with this treatment (1970). We later found

that the incidence of spontaneous obliteration among our large series of AVM was around 1%. I think that this first case of successful AVM treatment may have been one of them. “Gamma ligature” has not become a treatment strategy.
A real success for Gamma Knife surgery was one of the first patients ever treated for trigeminal neuralgia by targeting the trigeminal root entry zone. The patient had an immediate freedom of pain, which lasted. We now know that, rarely, an immediate and lasting freedom of pain may result, but more commonly it takes 2-6 months to achieve freedom of pain in Tic patients. Other remarkable “first ever” patients were the man with Parkinson’s disease who became tremor free 2 months after “Gamma thalamotomy” (1985), the young woman who became seizure free after Gamma Knife radiosurgery for her small low-grade glioma in the right medial temporal lobe, and the first reported success of Gamma Knife Surgery for a cerebral metastasis (1989). The metastasis was a recurrence 3 months after surgical removal of a renal cell carcinoma. Six months after the GKS the tumor had still not recurred, but the patient unfortunately succumbed to systemic disease.

And disasters?

Maybe the disasters haunt me more than the successes make me happy, so I can remember more disasters than I can remember successes, which speaks pretty well for radiosurgery because successes are very common, while disasters are a few but sometimes very devastating. One of the first cavernomas we treated was in a young, football player from Holland who played for the national team. He was one of the upcoming heroes of Dutch football. He had a brain stem cavernoma and I believe we treated him with a dose that we often used for AVMs but with a little reduction; 20 Gy. This had terrible consequences which left him wheelchair bound and I was haunted by this for years because I saw him on TV in his wheelchair on the sideline during a national game. There was another similar case which was a very beautiful model with a brainstem cavernoma referred from New York. She was left with a complete facial paralysis after the treatment. There were a few AVM cases: One I remember was a thalamic AVM that I treated together with Dr

Steiner and she developed radionecrosis and was left with a spastic hemiparesis which fortunately recovered pretty much, but was still devastating. The alternative treatment might have been worse.

So this might explain why those that were involved in the early radiosurgery program at the Karolinska are so reluctant to treat cavernomas?

Absolutely.

Are there any indications that you were first to treat?

The first report on Gamma Knife surgery for a metastatic tumor, which I just talked about. Our friend Volker Sturm from Heidelberg published first, treating with a linear accelerator, but, if I recall correctly, at the time they couldn't show any reduction of the tumor volume, but a stable situation. With Sten Håkansson, I started treating trigeminal neuralgia targeting the trigeminal nerve root. Together we presented 12 cases at the AANS meeting in Boston in 1993.
We had observed that for patients with AVM and focal epilepsy caused by the AVM related be cured of their seizure disorder even if their AVM didn't go away. This prompted me and Lars Kihlström to treat other patients with focal epilepsy by Gamma Knife surgery. In addition to stereotactic MRI we tried to use stereotactic magnetoencephalography to localise the epileptic foci, but unfortunately the software was very poor and localization therefore unsatisfactory. This was when MEG was in its infancy and the prototype machine we used had only 22-channels. Eventually we gave up on stereotactic MEG. We did treat 9 cases of focal epilepsy of various causes; low grade glioma, cerebral cortical malformation, stroke, and others.
I was also involved in the first cases of MR localisation for Gamma Knife radiosurgery, treating OCD and Parkinsonian tremor with Leksell. This was when we had access to the very first MRI scanner in Sweden, in Uppsala, 1985.

How were doses decided in those early days?
There's a description on how the doses were decided for AVMs which

we published in JNS with Steiner (our fellow John Adler was a co-author). It described the long term follow up of patients treated with radiosurgery. In the introduction, we describe what Steiner told us: That he had read a paper where they reported a patient with neck cancer exposed to a treatment dose of 25 Gy, which resulted in occlusion of the carotid artery. Hence this dose was used for AVM.
Some of the dose theories were worked out by Börje Larsson and the other early Gamma Knife pioneers (like Backlund), working with animals. The basis was roughly that as long as you don't harm the brain you can use whatever high dose was necessary. For instance, for ablation of the pituitary, they used up to 100 Gy or even 200Gy as treatment for severe diabetic retinopathy or intractable pain in terminal cancer patients. Doses for other pathologies were selected based on available tolerance doses for neighbouring eloquent tissue and data from animal studies.

Who do you regard as the genius in the field?

The inventor himself, Lars Leksell is outstanding. Lars Leksell was an innovator of unusual proportions, and we can see this from the other innovations that he has made (focussed ultrasound and brain ultrasound scanning). He was always full of ideas and sometimes he could not refrain from calling even early on Sunday morning to continue talking about an idea he presented the previous day and he was always full of new ideas. His collaborator and Gamma Knife co-inventor physicist Börje Larsson must also be mentioned in this context. Two other pioneers were the neurosurgeons Erik Olof Backlund and Ladislau Steiner. They were blessed by having access to a new tool before anybody else and they certainly made many and very significant contributions to the field. Whether they deserve the epithet genius is beyond me.

It must have been hard to work with Leksell in a way?

In a way, he was hard to work with because he was 'retired' and he could devote all his time to his favourite hobby which was the development of stereotaxy whereas we had to work very hard with clinical chores. Leksell could come into my office, put his feet on my

desk and start talking about his ideas. With over 30 years of an age difference, and his big authority, it was impossible to ask him to leave.

Is the technique ready for other techniques? Like ultrasound?

I think ultrasound is extremely interesting. I've been involved in consultancy work on this topic. Ten years ago, I was following the literature rather carefully. I believe ultrasound has a great potential as a lesion maker but also as an adjunct to other treatments. As you know, ultrasound has the possibility of opening the blood brain barrier which could help in delivering drugs to malignant tumours and other targets in the brain. If you talk about focussed ultrasound for the whole body, it is already accepted as a tool for uterine fibroids and other pathologies. I think it's something important for the future. It doesn't necessarily need to be delivered by stereotactic means if you are talking about targets outside the head.

What future do you envision in neurosurgery?

I think that the neurosurgeons have made mistakes in the past in that they are too focused on how they treat, not what they treat. To paraphrase Lars Leksell: No treatment is too refined to treat the delicate brain. Now radiosurgery is big - that may be gone in 20 years, we don't know. I think it's very important to keep developing your treatment tools, and have an open mind to new treatments even if it takes you away from traditional surgery.
Neurosurgeons should remember that the Russian neurosurgeon Serbinenko was the first one to treat aneurysms with an endovascular technique. Now in many countries endovascular procedures have been lost to neuroradiology. This is a good example of how you can lose a very interesting panorama of disease just because you're not willing to adapt to new tools.