EDITORIAL

Ultrasound-guided neurosurgery: experiences from 20 years of cross-disciplinary research in Trondheim, Norway

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PROGRESS in neurosurgery has often been based on inventions or advancements in medical technology. The introduction of silver clips by Cushing and later modification by McKenzie that significantly reduced surgical mortality, the Spitz-Holter shunt valve for treatment of hydrocephalus, and the numerous advancements in medical imaging technology such as CT and MRI are examples of medical technology that revolutionized diagnostics and neurosurgical treatment. The development of frame-based and later frameless neuronavigation based on preoperative imaging data and the development of intraoperative imaging based on ultrasound or MRI have also influenced the way neurosurgery is performed.

Although pioneering neurosurgeons are rightfully often given much credit for introducing various new tools that have led to significant improvements in treatment results, it should be remembered that progress often rests on technical developments based on close collaboration with engineers. The technology used in the operating room (OR) should ideally enhance the clinical results for a group of patients as a whole, simplify the procedure for the surgeon, be cost effective, and be well adapted to the workflow in the OR, for a given surgical procedure. At the same time, surgeons also need to be aware of the limitations of the technology and the implications for proper clinical use. As both neurosurgical procedures and medical technology are becoming more and more sophisticated, it is likely to be increasingly important to combine technological and clinical expertise to develop useful tools for neurosurgery.

In Trondheim, Norway, the surgeons at St. Olav's University Hospital (SOH) and technologists at the research foundation SINTEF and the Norwegian University of Science and Technology (NTNU) have collaborated for 20 years in the field of ultrasound-guided neurosurgery. We hereby briefly share our experience in how to set up a fruitful cross-disciplinary research team and present some

of the results obtained. We postulate that cross-disciplinary research between engineers and surgeons is the key to develop technology that will lead to better clinical results.

Ultrasound Imaging in Neurosurgery

Different technologies are used for image guidance in the surgical treatment of brain tumors—for example, low-field and high-field MRI, ultrasound imaging, and, more recently, fluorescence using 5-aminolevulinic acid for resection of high-grade gliomas.^{2,4,6,14,18} The use of ultrasound for imaging in neurosurgery has been promoted by several groups that have explored the use of B-mode and Doppler mode as well as elastography mode and contrast-enhanced ultrasound.^{7,13,16,21}

Cross-disciplinary research within ultrasound imaging has quite a long history in Trondheim. In the mid-1970s scientists at NTH (Norwegian Institute of Technology, now NTNU) and SINTEF started to develop ultrasound Doppler technology for cardiac examinations.¹ The engineers developed technology that the clinicians started to explore for clinical use in cardiology.⁸ This research activity led to the development of an ultrasound system within the company Vingmed Ultrasound (Horten, Norway), later bought by GE Healthcare in 1998.

The cross-disciplinary collaboration within ultrasound-guided neurosurgery started in the early 1990s when neurosurgeon and professor Geirmund Unsgård asked the technologists at SINTEF and NTNU about the possibility of using ultrasound for imaging of brain tumors during surgery. The ultrasound scanners were brought to the OR, and the ultrasound acquisition parameters were optimized for better imaging of brain tumors.²⁰ It was found, however, that the unfamiliar direction of the ultrasound image slices made it a bit challenging for the surgeons to interpret the anatomy shown in the ultrasound images. The

ABBREVIATIONS NTNU = Norwegian University of Science and Technology; OR = operating room; SOH = St. Olav's University Hospital.

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surgeons were more familiar with interpreting diagnostic MR images shown in patient-oriented slices (axial, coronal, and sagittal).

These limitations of real-time 2D ultrasound imaging were addressed with the use of optical tracking technology and frameless neuronavigation. Fixating a frame with spherical reflective markers onto the ultrasound probe enabled the acquisition of ultrasound images with position data that could be reconstructed into an image volume. The system allowed the surgeon to acquire a 3D ultrasound volume by tilting and translating the ultrasound transducer over the region of interest. The navigation software converted the 2D images into a 3D ultrasound volume that was stored on the computer. The ultrasound volumes could be displayed on the navigation system monitor as patient-oriented images (coronal, sagittal, and axial planes) or as reformatted arbitrary image slices, defined by the spatial position and orientation of the tracked tool. Moreover, the ultrasound volumes could be displayed along with corresponding image slices from preoperative MR data on the neuronavigation system, which also facilitated the interpretation of the ultrasound images.

These developments led to the first operation with 3D ultrasound in brain tumor surgery in 1996 at SOH. Since then, navigation technology with preoperative MRI and intraoperative 3D ultrasound has become standard procedure in almost all brain tumor surgeries at the hospital.^{5,19}

The methods developed in Trondheim were commercialized by the start-up company SonoWand AS (Trondheim, Norway). There are also other companies offering the integration of ultrasound imaging with navigation technology, including BK Medical (Herlev, Denmark), BrainLab (Feldkirchen, Germany), Esaote (Genoa, Italy), and companies offering methods for multimodal image fusion such as ImFusion (München, Germany).

The Potential Benefits of Collaboration Between Engineers and Surgeons

In every collaboration there should be a mutual benefit for all parties involved, including future patients. The surgeons and technologists should be jointly motivated by the possibility of developing surgical methods and technology that may improve patients' clinical outcome. A cross-disciplinary group may have a better chance of succeeding due to the simple fact that technologists bring technological expertise into the OR and clinicians bring their clinical expertise to the technological developments. The joint technology development may provide the surgeons with new and useful tools in the OR that might simplify surgery and provide better clinical results.

The cross-disciplinary collaboration may also open up for more joint scientific publication from the research groups. Pilot studies involving novel solutions and technology can be accepted in high-ranking scientific journals even if the number of patients is not very high. If the initial results are encouraging, there will be a need to validate the technology further through clinical trials. It is our experience that the collaboration between engineers and surgeons actually has triggered more clinical studies at the neurosurgical department. When developing technology for medical use, it is crucial to closely moni-

tor clinical results and possible adverse effects. Thus, the systematic registration of clinical data has contributed to the initiation of numerous important clinical studies, including studies proving improved survival in patients with low-grade gliomas undergoing early surgical resection, as well as quality-of-life studies.^{10,15}

Part of doing research is securing funding. Collaboration between engineers and clinicians can open new possibilities for financing research.

Technological and Clinical Collaboration—Some Practical Advice

In 2016, the collaboration at the current Norwegian National Advisory Unit for Ultrasound and Image-guided Therapy (USIGT) and its predecessors will have a 20-year anniversary for cross-disciplinary research in the field of ultrasound-guided neurosurgery. Clearly, not all collaboration is meant to, or even should, last for decades. However, there are some elements that in our opinion are important for building a lasting and hopefully successful collaboration between neurosurgeons and engineers. Some key issues are presented below (not necessarily in order of priority).

- Focus on technological and clinical developments that may contribute to solving clinical challenges. Better clinical outcome for the patient should be the joint core objective for all involved parties.
- Welcome the engineers to the OR. Observation is the only way that the engineers can understand more of the clinical challenges associated with the operations. This will likely prevent engineers from developing impressive technology that may not be usable in the clinical environment.
- Allocate time for communication and discussions—or you might risk having good ideas forgotten. At SOH the neurosurgeons and engineers meet at 11 AM every Friday and have done so for the last 19 years.
- The surgeons should be prepared and motivated to perform pilot studies involving the new technology. Of course, the technology should first be tested in the laboratory (in situ) and the necessary regulatory and ethical approvals must be obtained.
- The surgeon and the OR team must be willing to adjust the clinical procedure or the OR setup to facilitate the use of new technology. A time slot (agreed upon upfront) must be allocated for the testing of the technology.
- Patience and endurance are needed—development of new technology takes time and is usually an iterative process involving some degree of technological trial and error to become user-friendly and well adapted to the clinical procedures.
- The collaboration should focus on areas that you are already good at, both in the clinical and the technological field.
- Pursue incremental developments in the OR. Of course, the research groups should have exciting objectives for both short and longer time frames, involving laboratory work, preclinical trials, and clinical testing. However, the methods to be tested in the OR should represent a natural development of existing procedures and workflow. Radical concepts that imply reinventing the whole

OR as well as all established clinical procedures might not be easily applicable at other clinical centers. “Everybody wants something new, but nobody wants to change their habits” is a phrase to have in mind for the enthusiastic engineer and clinician. This is not the same as saying that you should focus on boring technology, just develop technology and procedures that are realistic in a real world.

- Be dynamic—invite other researchers and clinicians to contribute if they have expertise relevant to your joint endeavors.

It is very advantageous, perhaps even necessary, that the collaborating partners are located in close proximity (as we are in Trondheim) and have financing to support the collaboration.

Concluding Remarks and Suggestions for Further Actions

We believe that the concept of 2D and 3D ultrasound has an important role to play in the future of image-guided neurosurgery. Scanner and ultrasound probe technology is advancing steadily and we are still exploring methods and technology that can improve the concepts further and adapt the technology to a wider range of clinical procedures. Recent publications from other groups also show that there are many others exploring the use of ultrasound imaging in neurosurgery, and it is our impression that the clinical interest in using ultrasound for intraoperative brain imaging is steadily increasing.^{9,11–13,17}

To encourage more research in this field, we have launched the fully open source software CustusX as a research platform for ultrasound- and image-guided therapy.³ The software can be downloaded at www.custusx.org.

Furthermore, we are arranging annual courses on ultrasound imaging in neurosurgery to be held in Trondheim, Norway (see www.usigt.org). The goal of these courses is to teach neurosurgeons “best practice” on how to acquire good-quality images and how to interpret the ultrasound images. As with all technology and tools, the use of ultrasound requires that the surgeons are willing to learn the fundamental principles to have a good outcome.

We believe strongly in cross-disciplinary research as a means to develop medical technology for neurosurgery and we definitely encourage other groups of engineers and surgeons that have an interest in technology to team up in the quest for developing useful technology and methods to improve patient treatment. Open up your minds for cross-disciplinary collaboration and get to it!

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Disclosures

The authors report no conflict of interest.