FRONTIERS

Navigated High Frequency Ultrasound: Description of Technique and Clinical Comparison with Conventional Intracranial Ultrasound

Jan Coburger[1], Ralph W. König[1], Angelika Scheuerle[2], Jens Engelke[1], Michal Hlavac[1], Dietmar R. Thal[2], Christian Rainer Wirtz[1]

OBJECTIVE: **Conventional curved or sector array ultrasound (cioUS) is the most commonly used intraoperative imaging modality worldwide. Although highly beneficial in various clinical applications, at present the impact of linear array intraoperative ultrasound (lioUS) has not been assessed for intracranial use. We provide a technical description to integrate an independent lioUS probe into a commercially available neuronavigation system and evaluate the use of navigated lioUS as a resection control in glioblastoma surgery.**

METHODS: **We performed a prospective study assessing residual tumor detection after complete microsurgical resection using either cioUS or lioUS in 15 consecutive patients. We compared the imaging findings of both ultrasound modalities in 44 sites surrounding the resection cavity. The respective findings were correlated with the histopathologic findings of tissue specimen obtained from those sites.**

RESULTS: **Use of cioUS leaded to an additional resection in 9 patients, whereas lioUS detected residual tumor during all surgeries. A further resection was performed at 33 of 44 intraoperative sites (75%) based on results of lioUS alone. Resected tissue was solid tumor in 66% and infiltration zone in 34%. No false-positive or false-negative findings were seen using lioUS. There was no case of a tumor detection in cioUS combined with a negative finding in lioUS. The difference of imaging results between cioUS and lioUS was significant (sign test, $P < 0.001$).**

CONCLUSIONS: **lioUS can be used as a safe and precise tool for intracranial image-guided resection control of glioblastomas. It can be integrated in a commercially available navigation system and shows a significant higher detection rate of residual tumor compared with conventional cioUS.**

INTRODUCTION

Maximizing the extent of resection (EoR) while preserving neurological function is the main goal in glioma surgery. Several studies (4, 10, 13, 18, 19, 23, 33) have demonstrated an increased overall survival if EoR exceeds 95% of contrast-enhancing tumor. At present, to achieve this goal, intraoperative imaging has become standard practice in most neurosurgical centers. Most common imaging techniques to assess EoR during surgery are intraoperative magnetic resonance imaging (iMRI) and intraoperative ultrasound (ioUS). Intraoperative low and high-field MRI provide excellent tumor visualization and an update of neuronavigation intraoperatively (14, 15, 25, 31). However, iMRI is expensive and

Key words
- Cerebral tumor
- cioUS
- Extent of resection
- Glioma
- High frequency ultrasound imaging
- iMRI
- lioUS
- Ultrasound

Abbreviations and Acronyms
3D: 3-dimensional
cioUS: Conventional intraoperative ultrasound
EoR: Extend of resection
GBM: Glioblastoma multiforme
GTR: Gross total resection
iMRI: Intraoperative MRI
ioUS: Intraoperative ultrasound
lioUS: Linear array intraoperative ultrasound
MRI: Magnetic resonance imaging
WHO: World Health Organization

From the [1]Department of Neurosurgery and [2]Section of Neuropathology, University of Ulm, Günzburg, Germany

To whom correspondence should be addressed:
Jan Coburger, M.D.
[E-mail: jan.coburger@uni-ulm.de]

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interrupts the surgical workflow significantly for scanning and postprocessing of imaging. In a global perspective, ioUS is probably the most commonly used imaging tool for intraoperative resection control in glioma surgery. In contrast to iMRI, ioUS is an inexpensive and easily available imaging modality for resection control (3). In addition, in combination with neuronavigation, brain shift. which occurs, can be assessed and EoR maximized, which leads to improved survival after glioblastoma surgery (20, 22, 30).

At present published data concerning intraoperative intracranial applications of ioUS is based on conventional intraoperative ultrasound (cioUS) small sector or curved array transducers of 4 to 10 MHz. The major drawback of cioUS is a decrease in sensitivity and specificity during surgery due to its high vulnerability to artifacts. It has been shown that artifacts are minimized if the transducer can be placed directly on the region of interest. However, because of the cone-shaped ultrasound image, lesions directly below the transducer (e.g., a superficial cortical lesion), often cannot be adequately visualized (7). High frequency linear probes (lioUS) have an extraordinarily high tissue resolution. The intraoperative applicability of the technique has been shown for peripheral nerve surgery (12). With this application the tissue-differentiating properties of high resolution lioUS allow distinct evaluation of traumatic nerve lesions and facilitates intraoperative decision making (11). Bozinov et al. (2) showed the excellent image quality and resection control using lioUS for surgery of intramedullary cavernomas.

In the past linear array transducers for lioUS were not used for intracranial procedures due to limitations by craniotomy size and the low depth of penetration. In addition, ultrasound scan retrieval of the area suspected for residual tumor can be challenging without the use of neuronavigation (32). Use of lioUS in high grade glioma surgery was mentioned by Solheim et al. (26). They used a commercially available system combining neuronavigation and ultrasound (SonoWand, Sonowand, Trondheim, Norway). However, no comparison is made between conventional sector and the new linear array transducers.

At present to our knowledge the technique of manually registering a commercially available linear array transducer for lioUS in an independent neuronavigation system has not been described. With this set-up we performed a prospective study evaluating intraoperative tumor detection of lioUS with cioUS based on a histopathologic assessment.

METHODS

In our institution navigated cioUS is used on a routine basis in glioma surgery.

In the present prospective study we established a protocol to coregister a lioUS probe in the neuronavigation system and evaluated prospectively the results in the first 15 patients.

A total of 15 patients harboring a glioblastoma had surgery using navigated cioUS, and navigated lioUS to detect residual tumor. A detailed description of the patient population is provided in Table 1.

Intraoperative Set-Up

Patients were operated in a dedicated iMRI environment—a BrainSuite iMRI-Myiabi with a 1.5-T Magnetom Espree scanner (Siemens, Erlangen, Germany).

Table 1. Patient Characteristics

Age (mean, years)	62 (min 52—max 78)
Female %	47
Location of tumor	
Frontal	53%
Temporal	27%
Parietal	13%
Occipital	7%
Left-sided lesion	47%
Recurrent disease	13%

Patient registration to the neuronavigation system was performed using automatic registration (iPlan 3.0, Brainlab, Feldkirchen, Germany) on the basis of a short preoperative T_1 MPRAGE scan without contrast after fixation of the head in the Noras head coil (Noras, Erlangen, Germany).

The T_1 MPRAGE images were fused to preoperatively acquired images (T_1 +/− dadopentetic acid, T_2, flair) that had been used to plan tumor contours and resection volume.

MRI fusion with the registered ioUS was always performed with 3-dimensional (3D) data sets of 1-mm voxel size (MPRAGE [magnetization prepared rapid gradient echo]).

Ultrasound

Intraoperative ultrasound was performed with an iU22 xMatrix Ultrasound system (Philips, Amsterdam, The Netherlands).

Concerning cioUS, we routinely performed all intracranial ultrasounds with an X7-2 xMatrix array 3D probe (Philips). The transducer is a 3D matrix array probe with 2500 elements using a 7- to 2-MHz extended operating frequency range. Combined with adaptive imaging processing (XRES; Philips), it is a state of the art high resolution low frequency transducer. In the present study we are referring to the probe as the cioUS transducer.

To investigate image quality and to perform an intraoperative tissue assessment we evaluated the use of a lioUS transducer. We applied a L15-7io compact linear array transducer (Philips) with a phase array of 128 elements, 8 degrees of trapezoidal imaging and an effective aperture length of 23 mm. The transducer uses an extended frequency range of 15—7 MHz. Special features of the probe are adaptive imaging processing (XRES) and real-time spatial compound imaging (SonoCT; Philips). Because of the compact size of the 11 × 31 mm and hockey stick shape, an intracranial application is feasible as opposed to most other high resolution linear array transducers (Figure 1). In the present study the probe is referred to as lioUS transducer.

Navigated lioUS: Description of Registration

Registration of a sector or curved array ultrasound transducer for integration into an independent neuronavigation system is a well-established procedure (27). The manual integration of an independent linear array transducer poses unique challenges and to our knowledge it has not been described previously. Figure 1