Maximal safe resection of intrinsic brain tumors is a major prognostic factor for survival. Real-time intraoperative imaging tools, including ultrasound (US), are crucial for maximal resection of such tumors. Microbubbles (MBs) are clinically used in daily practice as a contrast agent for ultrasound and can be further developed to serve combined therapeutic and diagnostic purposes. To achieve this goal, Oddo et al. developed novel MBs conjugated to specific ligands to receptors which are overexpressed in brain tumors. These MBs are designed to target a tumor tissue, visualize it, and deliver therapeutic molecules into it. The objective of this study was to assess the biodistribution of the test items: We used MBs labeled with indocyanine green (MB-ICG) for visualization and MBs conjugated to a cyclic molecule containing the tripeptide Arg-Gly-Asp (RGD) labeled with ICG (MB-RGD-ICG) to target brain tumor integrins as the therapeutic tools. Male Sprague Dawley rats received a single dose of each MB preparation. The identification of the MB in various organs was monitored by fluorescence microscopy in anesthetized animals as well as real-time US for brain imaging. Equally sized control groups under identical conditions were used in this study. One control group was used to establish fluorescence background conditions (ICG), and two control groups were used to test autofluorescence from the test items (MBs and MB-RGD). ICG with or without MBs (naked or RGD-modified) was detected in the brain vasculature and also in other organs. The pattern, duration, and intensity of the fluorescence signal could not be differentiated between animals treated with ICG alone and animals treated with microbubbles MBs-ICG or MBs-RGD-ICG. Following MB injection, either naked or combined with RGD, there was a sharp rise in the Doppler signal within seconds of injection in the brain. The signal was mainly located at the choroid plexus, septum pellucidum, and the meninges of the brain. The signal subsided within a few minutes. Injection of saline or ICG alone to respective animals did not result in a similar raised signal. Following a single intravenous administration of MB-ICG and MB-RGD-ICG to rats, the MBs were found to be effectively present in the brain [1)].

Nowadays the role of microsurgical management of intrinsic brain tumors is to maximize the volumetric resection of the tumoral tissue, minimizing the postoperative morbidity.

Resection of intrinsic and extrinsic brain tumours requires an understanding of sulcal and gyral anatomy, familiarity with tissue consistency and tissue manipulation. As yet, these skills are acquired by observation and supervised manipulation during surgery, thus accepting a potential learning curve at the expense of the patient in a live surgical situation. A brain tumour model could ensure optimised manual skills and understanding of surgical anatomy acquired in an elective and relaxed teaching situation.

Freshly prepared agar-agar solution with different concentrations was added with highlighter ink and injected into fresh sheep brains. RESULTS: Hardened agar-agar solution formed masses comparable to malignant brain tumours. Variation of the agar-agar concentration influenced diffusion of agar-agar solution in the adjacent brain tissue. Higher concentrated agar-agar solutions formed sharply delimitated masses mimicking cerebral metastases and lower concentrated agar-agar solutions tended to diffuse into the adjacent cerebral tissue. Adding highlighter ink to the agar-agar solution produced fluorescence after blue light excitation comparable to the 5-ALA induced fluorescence of malignant glioma.

The described in vitro sheep brain tumour model is simple and realistic, available practically everywhere and cheap. Therefore, it could be useful for young neurosurgical residents to acquire basic neuro-oncological skills, experiencing properties of the cerebral brain texture and its haptic perception and to learn handling of neurosurgical equipment [2)].

1)

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2)

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