pISSN 2384-1095
eISSN 2384-1109

iMRI 2021;25:218-228

https://doi.org/10.13104/imri.2021.25.4.218

iMRI
Investigative Magnetic Resonance Imaging

Magnetic Resonance Imaging Meets Fiber Optics: a Brief Investigation of Multimodal Studies on Fiber Optics-Based Diagnostic / Therapeutic Techniques and Magnetic Resonance Imaging

Jong-ryul Choi, Sung Suk Oh

Medical Device Development Center, Daegu-Gyeongbuk Medical Innovation Foundation (DGMIF), Daegu, Korea

Review Article

Received: June 22, 2021
Revised: September 2, 2021
Accepted: September 17, 2021

Correspondence to:
Sung Suk Oh, Ph.D.
Medical Device Development Center, Daegu-Gyeongbuk Medical Innovation Foundation (DGMIF), 80, Cheombok-ro, Dong-gu, Daegu 41061, Korea.
Tel. +82-53-790-5615
Fax. +82-53-790-5519
E-mail: ssoh@dgmif.re.kr

Due to their high degree of freedom to transfer and acquire light, fiber optics can be used in the presence of strong magnetic fields. Hence, optical sensing and imaging based on fiber optics can be integrated with magnetic resonance imaging (MRI) diagnostic systems to acquire valuable information on biological tissues and organs based on a magnetic field. In this article, we explored the combination of MRI and optical sensing/imaging techniques by classifying them into the following topics: 1) functional near-infrared spectroscopy with functional MRI for brain studies and brain disease diagnoses, 2) integration of fiber-optic molecular imaging and optogenetic stimulation with MRI, and 3) optical therapeutic applications with an MRI guidance system. Through these investigations, we believe that a combination of MRI and optical sensing/imaging techniques can be employed as both research methods for multidisciplinary studies and clinical diagnostic/therapeutic devices.

Keywords: Magnetic resonance imaging; Fiber optics; Multimodal studies; Diagnostic techniques; Image-guided therapies

INTRODUCTION

Magnetic resonance imaging (MRI) diagnostic systems can acquire information about biological tissues and organs based on a magnetic field that resonates by irradiating radio frequency waves inside a strong magnetic field. Because of its non-invasiveness and negligible radiation exposure compared to conventional radiographic imaging instruments, MRI systems have been widely employed to diagnose diseases (1-3), guide images for interventional therapies (4-6), and study functions of organs (7-9). Conversely, owing to the strong magnetic field present inside the MRI system, it is difficult to introduce electrical devices and metallic components that exhibit ferromagnetism or paramagnetism to perform multimodal diagnostics or image-guided treatments. To overcome this challenge, several research groups have developed and

applied diagnostic/therapeutic tools and modalities that are suitable for use in MRI systems. For instance, research and clinical implementations on surgical robots for treating a patient remotely within a strong magnetic field (10, 11) and MRI-guided ultrasound ablation for tumor treatments (12-14) have actively progressed.

Advantages of using optical sensing, imaging, diagnosis, and treatment techniques include their low invasiveness, high resolution, and acquiring biomedical information using specialized functional optical probes. Therefore, optical sensing and imaging techniques are used in various applications ranging from *in vitro* diagnostics to clinical applications (15-18). Fiber optics are applied in medical sensors, endoscopes, and therapeutic probes because they provide high degrees of freedom to transfer and acquire light (19-21). With optical fibers composed of non-metal ends, they can be used even in the presence of strong magnetic fields. Therefore, studies that apply optical fibers in MRI systems and implement optical sensing and imaging in combination with MR images have been actively conducted from preclinical assays to clinical applications.

In this article, we explored optical sensing, imaging, diagnostic, and therapeutic techniques based on fiber optics integrated with MRI by classifying them into the following topics: 1) functional near-infrared spectroscopy (*f*NIRS) with functional MRI (*f*MRI) for brain studies and brain-related disease diagnoses, 2) integration of fiber-optic molecular imaging and optogenetic stimulation with MRI, and 3) optical therapeutic applications with MRI guidance. Recent studies conducted on each topic were investigated. Additional techniques required for interdisciplinary studies in fields of MRI and optical sensing/imaging are summarized in the section of concluding remarks. Through this investigation, we expect that the combination of MRI and optical sensing/imaging techniques can be used as effective research methods and clinical diagnostic/therapeutic techniques.

Functional Near-Infrared Spectroscopy with MRI for Brain Studies

Functional near-infrared spectroscopy (*f*NIRS) is a brain imaging modality that measures oxy-, deoxy-, and hemoglobin concentrations in specific brain regions using near-infrared light with multiple wavelengths (22-25). Information acquired by *f*NIRS is mainly related to blood oxygenation level-dependent (BOLD) signals provided by *f*MRI, which obtains information about cerebral activities and functions of a particular brain region using MRI (26). Compared with *f*MRI, *f*NIRS is advantageous in terms of having a higher temporal resolution and ability to simultaneously analyze oxy-, deoxy-, and hemoglobin concentrations. Conversely, advantages of *f*MRI include its higher spatial resolution, the ability to acquire structural brain images and map them together, pre-existing literature, and rationale for utilization in brain research. *f*NIRS instruments that consist of fiber optics coupled with infrared light sources and photodetectors can simultaneously measure hemoglobin concentrations using *f*MRI. This indicates that both *f*NIRS and *f*MRI can provide cross-validated information about brain activity without compromising their respective advantages. Therefore, combined *f*NIRS-*f*MRI has been utilized in various applications, including studying brain functions, exploring brain disease diagnostic indicators, and validating treatment/rehabilitation techniques as follows.

Gagnon et al. (27) have performed concurrent *f*NIRS-*f*MRI measurements to classify hemodynamic responses in the cortex from *f*NIRS signals mixed with hemoglobin dynamics in blood vessels in the cortex and a pial surface. Cortical contributions in oxy-/deoxy- and total hemoglobin in *f*NIRS were analyzed with a combined result of Monte Carlo simulation using structural/angiographic MR brain images and *f*NIRS-*f*MRI measurements through motor stimulations. Duan et al. (28) have combined *f*NIRS and *f*MRI to analyze and compare the functional connectivity of the resting-state brain. Additionally, studies have been conducted to converge and explore associations of data acquired through *f*NIRS and *f*MRI while maintaining high temporal and spatial resolution (29, 30). Funane et al. (31) have validated a novel technique for obtaining *f*NIRS signals at several depths by placing light sources and photodetectors at different distances using concurrent *f*NIRS-*f*MRI. Liu et al. (32) have applied *f*NIRS and *f*MRI to analyze functional hemodynamics in a brain region associated with verbal communication and speech comprehension by listeners. When two subjects measured by *f*NIRS and *f*MRI, respectively, heard the same story, hemodynamics measured by *f*NIRS and BOLD *f*MRI showed a high correlation. However, when two listeners heard different stories, the hemodynamics had no significant correlation as shown in Figure 1. Based on such study, deriving the relationship between hemodynamics measured by *f*NIRS and BOLD *f*MRI signals and acquiring a highly relevant brain region for specific brain functions can be utilized to analyze brain activities and functions in various scenarios.

Research has also been actively conducted to use *f*NIRS

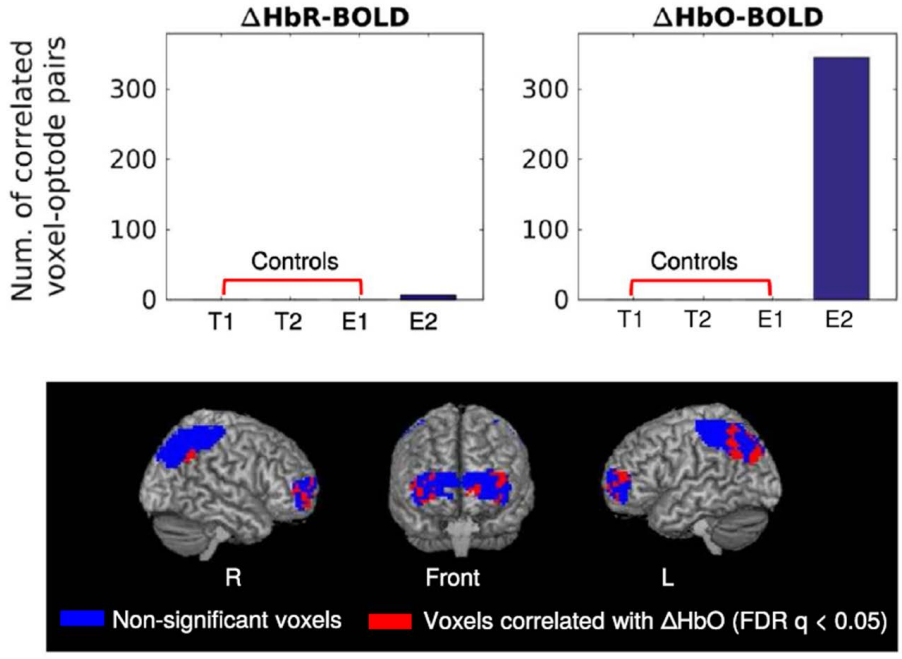


Fig. 1. An application of functional near-infrared spectroscopy with structural/functional magnetic resonance imaging to establish a correlation between hemodynamics acquired when a listener heard the story of E2 during *f*MRI measurement. Oxygenated hemoglobin dynamics measured by *f*NIRS indicated a high correlation with BOLD *f*MRI when the listener heard the story of E2. However, in the case of other languages or stories, there was no significant correlation between BOLD *f*MRI signals and hemoglobin dynamics measured by *f*NIRS. The map below shows the result of exploring brain regions with a high correlation (red) and no significant correlation (blue) between oxygenated hemoglobin dynamics captured by *f*NIRS and BOLD *f*MRI in this experiment. ΔHbO-BOLD indicates a correlation between changes in BOLD *f*MRI signals and oxygenated hemoglobin measured by *f*NIRS. ΔHbR-BOLD indicates a correlation between changes in BOLD *f*MRI signals and deoxygenated hemoglobin measured by *f*NIRS. Deriving the relationship between hemodynamics measured by *f*NIRS and BOLD *f*MRI signals and acquiring a highly relevant brain region for the specific brain functions could be utilized to analyze brain activities and functions in more various scenarios compared with using MRI only. Reprint of figures in (32) is permitted by Springer Nature under the terms of the Creative Commons CC BY license.

as a medical diagnostic device for brain disorders using simultaneous measurement and correlation analysis of *f*NIRS and fMRI. As a representative study, Amyot et al. (33) have investigated a technique to analyze and diagnose cerebrovascular damage after traumatic brain injuries using *f*NIRS and *f*MRI. Furthermore, Matarasso et al. (34) have established a system that combines real-time fNIRS and *f*MRI for feedback to promote motor function recovery after a stroke (34, 35). Integration and application of rehabilitation modalities such as volitional wrist extension training or functional electrical stimulations with the real-time *f*NIRS-*f*MRI system have the potential to improve recovery in stroke patients.

Integration of Fiber-Optic Molecular Imaging and Stimulation for MRI

MRI is an important research tool for noninvasive acquisition of structural images and BOLD functional MR images in preclinical studies of brain functions (36-38). Optical indicators such as calcium indicators (39, 40) and voltage-sensitive dyes (41, 42) can represent activities in certain parts of the brain. Furthermore, they can be applied to animal models for neuroimaging in preclinical studies (43-45). In preclinical brain studies, MRI has advantages of acquiring whole brain images and low invasiveness without special imaging probes. Optical sensing and imaging can obtain high-resolution neural information that is difficult to acquire using MRI. Merits in each modality are complementary to brain studies. To obtain concurrent information by optical measurements and MR imaging,

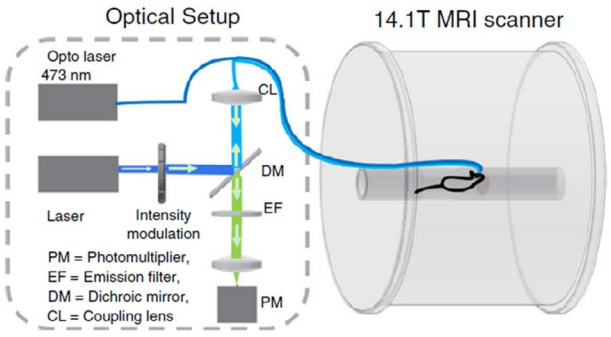
several research instruments have been developed by inserting optical fibers into MRI systems. Preclinical brain studies using these tools have been conducted by several research groups as follows.

Schulz et al. (46) have developed fiber-optic probes and a coil system that can be mounted inside the MRI system. They then conducted a study to simultaneously measure calcium flux using structural and *f*MRI in conjugation with an optical setup for fluorescence signal acquisition (46). By analyzing changes in BOLD *f*MRI and calcium flux caused by stimulation of the forepaw and hind paw, this study has confirmed that the fiber-optic calcium flux measurement setup is a potential tool to study brain function in conjugation with *f*MRI (46). Liang et al. (47) have developed a fiber-coupled photometry to measure GCaMP6, a genetically encoded fluorescent calcium indicator, of a selected region in a rat brain with the acquisition of BOLD *f*MRI. In their study, an additional optical fiber was inserted into the MRI system for visual stimulation and changes in calcium flux and BOLD signals were measured simultaneously by visual stimulation. It was observed that there was a time difference between the peak of calcium flux and BOLD signals for each rodent after visual stimulation. Therefore, fiber-coupled photometry can be potentially used to understand various neural activities. Schlegel et al. (48) have established a method of acute/chronic fiber-optic probe implementation, a method of MRI-integrated fluorescence signal acquisition, and protocols that can simultaneously record calcium flux-related fluorescence signals and high-resolution BOLD *f*MRI. Studies have been conducted to obtain multidimensional cerebral calcium flux-related fluorescence images with BOLD *f*MRI by inserting an imaging fiber bundle consisting of multiple optical fibers inside an MRI system. As a representative study, Lake et al. (49) have developed a system that can simultaneously acquire the BOLD *f*MRI of the entire brain and fluorescence calcium flux images in multiple cerebral cortices using an imaging fiber bundle. The fiber bundle consisting of two million optical fibers was implemented in an MRI system (49). Results obtained by simultaneous acquisition of BOLD *f*MRI and fluorescence calcium flux images using the system and correlation analysis demonstrated the potential of utilizing fiber-based fluorescence imaging integrated with an MRI instrument for in-depth study of brain functions and cortical connectivity in rodents.

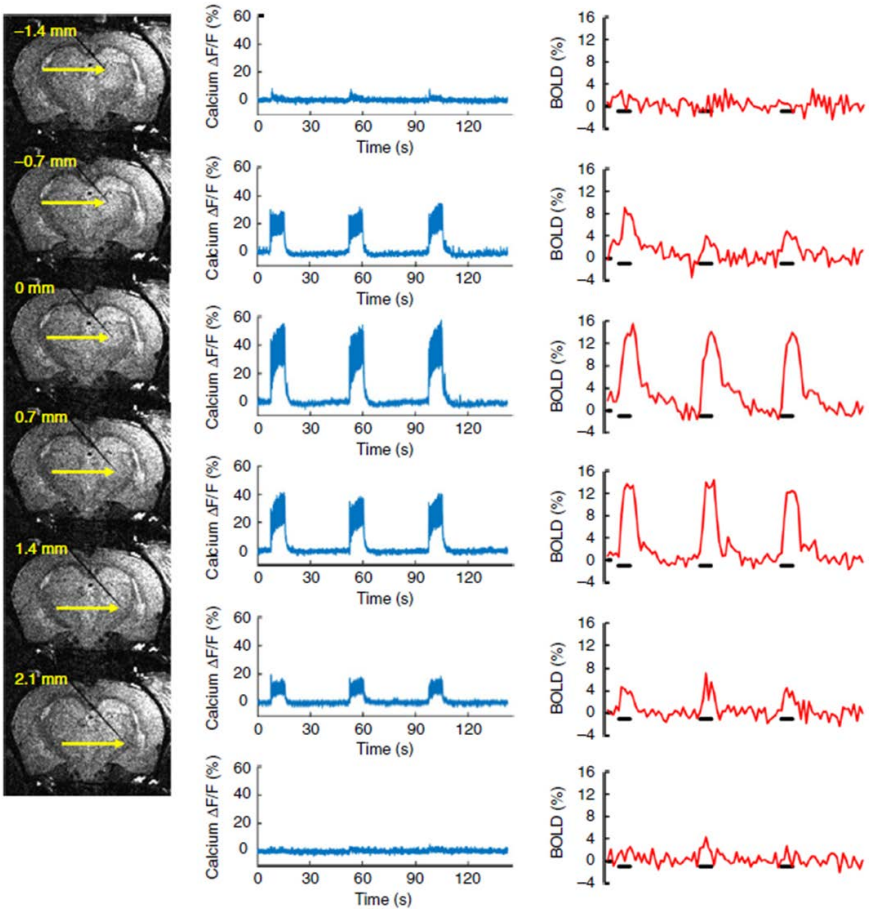
In vivo animal studies that use light to stimulate neurons in specific brain regions and analyze responses, functions in the selected area, and connectivity using high-resolution BOLD *f*MRI are mostly based on optogenetics, a novel biological technique that utilizes specific wavelengths of light to control genetically modified neurons (open or closed) to express light-sensitive ion channels (50-52). It is possible to explore brain function and connectivity by mounting fiber-optic probes in a specific brain region for genetically modified animal models and simultaneously performing optogenetic stimulation and BOLD *f*MRI of the entire brain. Desai et al. (53) have investigated a mountable fiber optic probe capable of delivering blue light to a mouse brain in a holder of an MRI system and analyzed changes in BOLD signals in each region caused by optogenetic neural stimulation in the primary somatosensory cortex and brain connectivity that can be estimated. This opto-*f*MRI has been actively applied by several research groups in neuroscience to understand brain functions and responses to localized neural stimulation in various parts of the brain (54-58). In addition, optogenetic neural stimulation and fluorescence measurements can be independently combined by diverging light from the fiber or adding additional optical fibers in the configuration of optical systems outside the MRI system. Chen et al. (59) have investigated a fiber-optic system for fluorescence calcium flux recording and optogenetic stimulations. They combined the system with an MR-compatible robotic arm to deliver optogenetic stimulations and obtain fluorescence signals in a certain position as shown in Figure 2 (59). Furthermore, Chen et al. (60) have developed an optical platform to simultaneously perform optogenetic neural stimulations, fluorescence calcium recording, and BOLD *f*MRI acquisitions of the entire brain by attaching a 473-nm laser light source to a fiber-optic fluorescence calcium flux measurement setup.

Optical Therapeutic Applications with a Guidance of MRI

MRI can be applied to image guides for precise treatments because it can noninvasively monitor tissues and organs inside the body. Hence, treatments using MR-compatible surgical robots, which can be guided using MRI, are actively being conducted from applied research to commercialization (10, 11, 61). Optical therapeutic techniques have advantages of high resolution and minimal invasiveness due to small sizes of fiber optic probes inserted. Therefore, they can be operated inside an MRI system. In this section, we investigated two optical techniques to perform precise treatment under the guidance of MR images. The first technique is MR-guided laser interstitial



a



b

Fig. 2. (a) A schematic of a fiber-optic system for optogenetic stimulations and fluorescence calcium flux measurements. Connections between the optical fiber and a MR-compatible robotic arm device allow the fiber-optic probe to be precisely introduced into specific areas of the rodent brain. (b) Responses of fluorescence calcium flux and BOLD *f*MRI signals to stimuli at different locations, which can be identified by anatomical rapid acquisition with relaxation enhancement (RARE) MR images (on the left side of Fig. 2b). The reprint of figures in (59) is permitted by Springer Nature under the terms of the Creative Commons CC BY license.

thermal therapy (MRgLITT) to treat brain diseases. The second technique is MR-guided photodynamic therapy (PDT).

The MRgLITT technique is used for precise cauterization of tumors using light, especially brain tumors, leading to subsequent release of thermal energy focused at the end of the fiber-optic probe (62). MRgLITT uses this thermal energy to denature tumor proteins and remove them. In MRgLITT, MRI provides structural brain images and tumor locations. It also precisely monitors brain tissue temperature changes during laser irradiation to eliminate side effects such as denaturation of normal tissue due to excessive laser output (63). Schwarzmaier et al. (64, 65) have applied MRgLITT using a system consisting of fiber-optic probes with a diffuser end, a continuous wave laser

source with a central wavelength of 1064 nm, a 0.5T MRI, and a navigation instrument to patients with recurrent glioblastomas and investigated the duration of survival and tumor size reduction. Carpentier et al. (66) have employed MRgLITT to treat metastatic intracranial tumors resistant to conventional treatments. In this clinical application, optical fiber probe designed to rapidly cool the probe and brain tissues by circulating sterile saline on the outer portion of the probe was used. Additionally, a tool called 'cranial anchor' allows the probe in accurately accessing tumor locations. Furthermore, MR thermometry and contrast agent (gadolinium) augmented T1-weighted MR images have been employed for precise laser interstitial thermal therapy. Hawasli et al. (67) have performed clinical MRgLITT for intracranial lesions using a probe that can irradiate the laser orthogonally. The effectiveness of MRgLITT was verified using T1/T2-weighted MRI and single photon emission computed tomography (SPECT) images (67). In addition, studies have been actively conducted to clinically apply MRgLITT for the treatment of brain tumors, which cannot be removed by anti-cancer drugs, radiation therapy, or conventional surgery (68-71).

MRgLITT is also used as a substitute of brain surgery for treating epilepsy based on precise cranial tissue cautery (66, 72, 73). As a representative clinical application, Gupta et al. (74, 75) have applied a robot-assisted, stereotactic MRgLITT to treat extratemporal lobe epilepsy as described in Figure 3. Through the application of MRgLITT to 35 patients, MRgLITT as a safe and effective modality for treating extratemporal lobe epilepsy has been demonstrated.

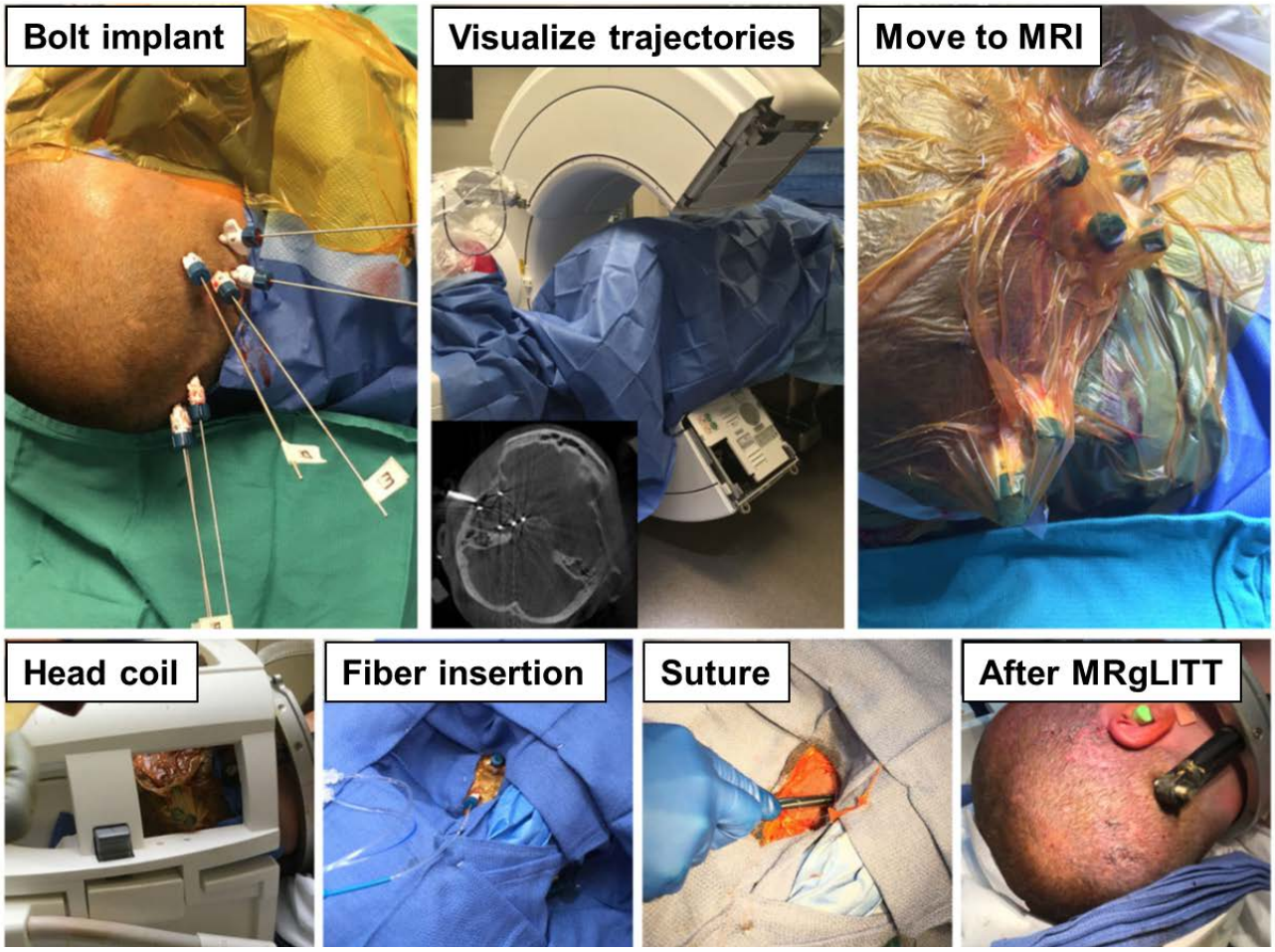
PDT is a technique used to treat abnormal cells locally (such as carcinomas) using reactive substances containing photosensitive chemicals (76, 77). PDT treats the disease by activating oxygen to directly eliminate abnormal cells or block blood supplies connected to abnormal cells to prevent nourishment. Precise light irradiation to the location of lesions and activation of the photosensitizer are important in the practical application of PDT in clinical settings. Therefore, MRI-guided PDT has been developed for accurate PDT applications. Several research groups have verified MRI-guided PDT in the preclinical research phase.

Gross et al. (78) have established PDT, which blocks blood supply to induce the death of melanoma. This treatment method was confirmed by applying optical fiber-based light irradiation inside an MRI system with simultaneous measurements of BOLD MR images (78). Researchers have used palladium-bacteriopheophorbide as a photosensitive agent of PDT and confirmed through MRI that palladium-bacteriopheophorbide with near-infrared light can reduce BOLD MR signals by 25% to 40% in the region of melanoma (78). Leroy et al. (79) have investigated a technique to simultaneously monitor the application of PDT to treat brain tumors using diffusion and perfusion MRI. Bechet et al. (80) have developed a multifunctional nano-agent with a photosensitizer and an MR contrast agent to perform PDT-based brain tumor treatments using an MRI guidance system. They confirmed that the nano-agent could be used to simultaneously acquire highly sensitive MR imaging while performing PDT-based treatment of brain cancer tissue. Furthermore, Xie et al. (81) have developed a manganese-doped layered double hydroxide nanoparticle-based PDT agent that can induce cancer tissue necrosis in response to light with a central wavelength of 808 nm and a platform to expose light while receiving a guide to MRI.

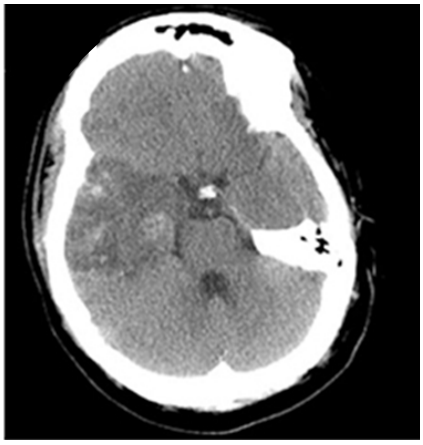
Concluding Remarks

In this article, fiber-optic sensing, imaging, diagnostic, and therapeutic techniques integrated with MRI are described. A combination of *f*NIRS and *f*MRI has potential applications in various research and biomedical fields, such as neuroscience, brain disease diagnosis, and treatment efficiency validation. The main advantage of combining *f*NIRS and *f*MRI is that each signal from these two modalities is independent of each other without any interference. In addition, because *f*MRI has a higher spatial resolution than *f*NIRS while *f*NIRS has a higher temporal resolution than *f*MRI, simultaneous measurement allows these two modalities to complement each other. In addition, fNIRS could be applied to more diverse scenarios for brain function analysis due to its low spatial constraints such as magnetic field shielding in MRI. When a significantly correlated brain region is established in cognitive tasks using the relationship between hemoglobin dynamics and BOLD signals by *f*NIRS and *f*MRI, respectively, a brain function analysis with a highly improved degree of freedom could be possible using *f*NIRS with mobility.

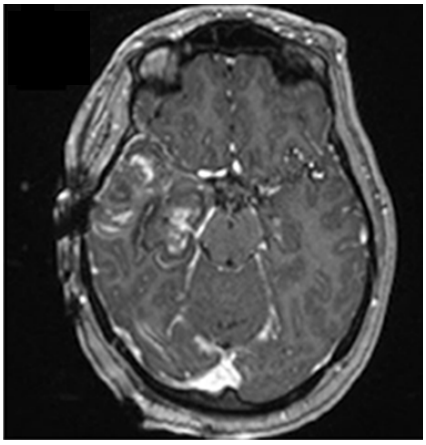
Considering these points, further implementation with MR-compatible electroencephalography is expected to provide better information (82, 83). Studies that find correlation between *f*NIRS and *f*MRI through machine learning (84) can increase the feasibility of neuroimaging for brain function studies and medical applications. Fluorescence signal/image acquisition and optical brain stimulation using fiber-optic probes integrated with MRI systems have been applied to preclinical studies of small animals. The integration of optical fiber-based fluorescence



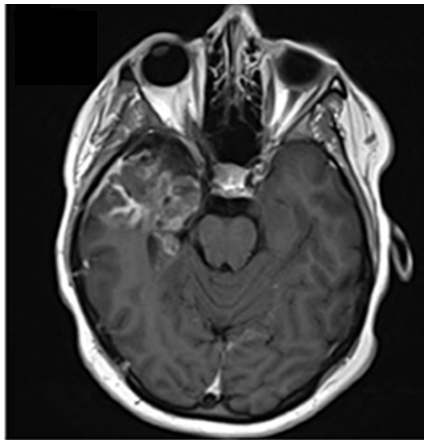
a



b



c



d

Fig. 3. (a) Overall procedure of MR-guided laser interstitial thermal therapy (MRgLITT) to treat temporal lobe epilepsy. (b) A computer tomographic (CT) image of a patient brain at two days after treatment using robot-assisted MRgLITT. Contrast-enhanced T1 images (c) at the time of the treatment using MRgLITT and (d) at three months after the treatment. In an observation over three months following the treatment, an intense perineural enhancement of nerves was observed. Figures shown in (75) are reprinted with the permission from Frontiers Media S. A. under the terms of the Creative Commons Attribution License (CC BY).

signal acquisition into MRI has the merit of simultaneously obtaining fluorescence-based biomolecular information on high-resolution structural and functional brain MRI. Optogenetic brain stimulation using fiber optics enables activation and deactivation of local brain regions using light. It can be applied as a great modality to identify the function and connectivity of specific brain regions in conjugation with MRI. Conversely, for utilization as a general-purpose research equipment, an imaging optical fiber, which consists of a bundle of optical fibers, is necessary to solve the high cost and difficulty in setting up the system. In addition, before applying fluorescence signal acquisition and optogenetic brain stimulation to clinical studies, the safety of optogenetic probes and fluorescent indicators must be verified. When additional system development, optimization, and preclinical applications are undertaken, these techniques can be employed in neuroscience research for large animals and advanced medical technologies such as optical stimulation-based brain-machine interfaces (85). MRgLITT, an optical tumor treatment with an MRI guidance system, has been used for the ablation of small brain tumors that cannot be treated using drugs or radiation therapy. MRgLITT has the advantage of being a minimally invasive brain tumor treatment compared with general surgeries. In particular, it can reduce the risk of treatment by a guide from brain MR images before and after tumor treatment. High-speed acquisition of MR images, the development of advanced MR sequences, and post-processing algorithms to analyze therapeutic effect can help active clinical applications of MRgLITT. In addition, the high cost of establishing a system of MRgLITT and the lack of sufficient clinical cases should be overcome for active utilization in clinical areas such as treatment of brain tumors. We propose that a combination of MRI and optical sensing/imaging techniques can be effectively used as a brain research modality and medical diagnostic/therapeutic technique.

Acknowledgments

This study was supported from a grant (NRF-2020R1C1C1012230) of the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science & ICT. This work was also supported by a grant (HI17C1501) of the Health Technology R&D Project through the Korea Health Industry Development Institute (KHIDI) funded by the Ministry of Health & Welfare, Republic of Korea.

REFERENCES

1. Park JK, Hong DY, Jin ST, Lee DW, Pyun HW. Leak sign on dynamic-susceptibility-contrast magnetic resonance imaging in acute intracerebral hemorrhage. Investig Magn Reson Imaging 2020;24:154-161
2. Jung DY, Lee EJ, Bae JM, Choi YJ, Lee, EK, Kim DB. Differentiation between glioblastoma and solitary metastasis: morphologic assessment by conventional brain MR imaging and diffusion-weighted imaging. Investig Magn Reson Imaging 2021;25:23-34
3. Oh CH, Kang WY, Lee OJ. Langerhans cell histiocytosis of the rib of an adult female patient: a case report. Investg Magn Reson Imaging 2020;24:61-65
4. Rosenberg SA, Henke LE, Shaverdian N, et al. A Multi-Institutional Experience of MR-Guided Liver Stereotactic Body Radiation Therapy. Adv Radiat Oncol 2019;4:142-149
5. Wang W, Dumoulin CL, Viswanathan AN, et al. Real-time active MR-tracking of metallic stylets in MR-guided radiation therapy. Magn Reson Med 2015;73:1803-1811
6. Cash RFH, Cocchi L, Lv J, Fitzgerald PB, Zalesky A. Functional Magnetic Resonance Imaging-Guided Personalization of Transcranial Magnetic Stimulation Treatment for Depression. JAMA Psychiatry 2021;78:337-339
7. Pozzi E, Vijayakumar N, Rakesh D, Whittle S. Neural Correlates of Emotion Regulation in Adolescents and Emerging Adults: A Meta-analytic Study. Biol Psychiatry 2021;89:194-204
8. Seo HS, Jang KE, Wang D, Kim IS, Chang Y. Accelerated resting-state functional magnetic resonance imaging using multiband echo-planar imaging with controlled aliasing. Investig Magn Reson Imaging 2017;21:223-232
9. Hassel S, Sharma GB, Alders GL, et al. Reliability of a functional magnetic resonance imaging task of emotional conflict in healthy participants. Hum Brain Mapp 2020;41:1400-1415
10. Meinhold W, Martinez DE, Oshinski J, Hu AP, Ueda J. A direct drive parallel plane piezoelectric needle positioning robot for MRI guided intraspinal injection. IEEE Trans Biomed Eng 2021;68:807-814
11. Kim Y, Cheng SS, Diakite M, Gullapalli RP, Simard JM, Desai JP. Toward the development of a flexible mesoscale MRI-compatible neurosurgical continuum robot. IEEE Trans Robot 2017;33:1386-1397
12. Ghai S, Finelli A, Corr K, et al. MRI-guided focused ultrasound ablation for localized intermediate-risk prostate cancer: early results of a phase II trial. Radiology 2021;298:695-703
13. LeBlang SD, Hoctor K, Steinberg FL. Leiomyoma shrinkage

after MRI-guided focused ultrasound treatment: report of 80 patients. AJR Am J Roentgenol 2010;194:274-280
14. Pauly KB, Diederich CJ, Rieke V, et al. Magnetic resonance-guided high-intensity ultrasound ablation of the prostate. Top Magn Reson Imaging 2006;17:195-207
15. H?hne J, Schebesch KM, Zoubaa S, Proescholdt M, Riemenschneider MJ, Schmidt NO. Intraoperative imaging of brain tumors with fluorescein: confocal laser endomicroscopy in neurosurgery. Clinical and user experience. Neurosurg Focus 2021;50:E19
16. Sun Y, Hatami N, Yee M, et al. Fluorescence lifetime imaging microscopy for brain tumor image-guided surgery. J Biomed Opt 2010;15:056022
17. Ahn H, Song H, Shin DM, Kim K, Choi J. Emerging optical spectroscopy techniques for biomedical applications - a brief review of recent progress. Appl Spectrosc Rev 2018;53: 264-278
18. Choi JR, Song H, Sung JH, Kim D, Kim K. Microfluidic assay-based optical measurement techniques for cell analysis: a review of recent progress. Biosens Bioelectron 2016;77:227-236
19. Zou Y, Chau FS, Zhou G. Ultra-compact optical zoom endoscope using solid tunable lenses. Opt Express 2017;25:20675-20688
20. He Z, Zhou L, Luo B, Hu B, Du X, Li Y. Multifunction medical endoscope system with optical fiber temperature sensor. Proc SPIE 2014:9216
21. Nedoma J, Kepak S, Fajkus M, et al. Magnetic Resonance Imaging Compatible Non-Invasive Fibre-Optic Sensors Based on the Bragg Gratings and Interferometers in the Application of Monitoring Heart and Respiration Rate of the Human Body: A Comparative Study. Sensors (Basel) 2018;18
22. Bunce SC, Izzetoglu M, Izzetoglu K, Onaral B, Pourrezaei K. Functional near-infrared spectroscopy. IEEE Eng Med Biol Mag 2006;25:54-62
23. Scholkmann F, Kleiser S, Metz AJ, et al. A review on continuous wave functional near-infrared spectroscopy and imaging instrumentation and methodology. Neuroimage 2014;85 Pt 1:6-27
24. Ferrari M, Quaresima V. A brief review on the history of human functional near-infrared spectroscopy (fNIRS) development and fields of application. Neuroimage 2012;63:921-935
25. Nguyen HD, Hong KS, Shin YI. Bundled-Optode Method in Functional Near-Infrared Spectroscopy. PLoS One 2016;11:e0165146
26. Steinbrink J, Villringer A, Kempf F, Haux D, Boden S, Obrig H. Illuminating the BOLD signal: combined fMRI-fNIRS studies. Magn Reson Imaging 2006;24:495-505
27. Gagnon L, Yucel MA, Dehaes M, et al. Quantification of the cortical contribution to the NIRS signal over the motor cortex using concurrent NIRS-fMRI measurements. Neuroimage 2012;59:3933-3940
28. Duan L, Zhang YJ, Zhu CZ. Quantitative comparison of resting-state functional connectivity derived from fNIRS and fMRI: a simultaneous recording study. Neuroimage 2012;60:2008-2018
29. Yuan Z, Ye J. Fusion of fNIRS and fMRI data: identifying when and where hemodynamic signals are changing in human brains. Front Hum Neurosci 2013;7:676
30. Chen M, Blumen HM, Izzetoglu M, Holtzer R. Spatial Coregistration of Functional Near-Infrared Spectroscopy to Brain MRI. J Neuroimaging 2017;27:453-460
31. Funane T, Sato H, Yahata N, et al. Concurrent fNIRS-fMRI measurement to validate a method for separating deep and shallow fNIRS signals by using multidistance optodes. Neurophotonics 2015;2:015003
32. Liu Y, Piazza EA, Simony E, et al. Measuring speaker-listener neural coupling with functional near infrared spectroscopy. Sci Rep 2017;7:43293
33. Amyot F, Kenney K, Spessert E, et al. Assessment of cerebrovascular dysfunction after traumatic brain injury with fMRI and fNIRS. Neuroimage Clin 2020;25:102086
34. Matarasso AK, Rieke JD, White K, Yusufali MM, Daly JJ. Combined real-time fMRI and real time fNIRS brain computer interface (BCI): Training of volitional wrist extension after stroke, a case series pilot study. PLoS One 2021;16:e0250431
35. Rieke JD, Matarasso AK, Yusufali MM, et al. Development of a combined, sequential real-time fMRI and fNIRS neurofeedback system to enhance motor learning after stroke. J Neurosci Methods 2020;341:108719
36. Behroozi M, Helluy X, Strockens F, et al. Event-related functional MRI of awake behaving pigeons at 7T. Nat Commun 2020;11:4715
37. Jung WB, Shim HJ, Kim SG. Mouse BOLD fMRI at ultrahigh field detects somatosensory networks including thalamic nuclei. Neuroimage 2019;195:203-214
38. Grandjean J, Canella C, Anckaerts C, et al. Common functional networks in the mouse brain revealed by multi-centre resting-state fMRI analysis. Neuroimage 2020;205:116278
39. Kaszas A, Szalay G, Slezia A, et al. Two-photon GCaMP6f imaging of infrared neural stimulation evoked calcium signals in mouse cortical neurons in vivo. Sci Rep 2021;11:9775
40. Yang Y, Liu N, He Y, et al. Improved calcium sensor GCaMP-X overcomes the calcium channel perturbations induced by the calmodulin in GCaMP. Nat Commun

2018;9:1504
41. Knopfel T, Song C. Optical voltage imaging in neurons: moving from technology development to practical tool. Nat Rev Neurosci 2019;20:719-727
42. Kannan M, Vasan G, Huang C, et al. Fast, in vivo voltage imaging using a red fluorescent indicator. Nat Methods 2018;15:1108-1116
43. Kunori N, Takashima I. An Implantable Cranial Window Using a Collagen Membrane for Chronic Voltage-Sensitive Dye Imaging. Micromachines (Basel) 2019;10
44. Cramer JV, Gesierich B, Roth S, Dichgans M, During M, Liesz A. In vivo widefield calcium imaging of the mouse cortex for analysis of network connectivity in health and brain disease. Neuroimage 2019;199:570-584
45. Takashima I, Ichikawa M, Iijima T. High-speed CCD imaging system for monitoring neural activity in vivo and in vitro, using a voltage-sensitive dye. J Neurosci Methods 1999;91:147-159
46. Schulz K, Sydekum E, Krueppel R, et al. Simultaneous BOLD fMRI and fiber-optic calcium recording in rat neocortex. Nat Methods 2012;9:597-602
47. Liang Z, Ma Y, Watson GDR, Zhang N. Simultaneous GCaMP6-based fiber photometry and fMRI in rats. J Neurosci Methods 2017;289:31-38
48. Schlegel F, Sych Y, Schroeter A, et al. Fiber-optic implant for simultaneous fluorescence-based calcium recordings and BOLD fMRI in mice. Nat Protoc 2018;13:840-855
49. Lake EMR, Ge X, Shen X, et al. Simultaneous cortex-wide fluorescence Ca(2+) imaging and whole-brain fMRI. Nat Methods 2020;17:1262-1271
50. Nagel G, Szellas T, Huhn W, et al. Channelrhodopsin-2, a directly light-gated cation-selective membrane channel. Proc Natl Acad Sci U S A 2003;100:13940-13945
51. Kim CK, Adhikari A, Deisseroth K. Integration of optogenetics with complementary methodologies in systems neuroscience. Nat Rev Neurosci 2017;18:222-235
52. Song C, Knopfel T. Optogenetics enlightens neuroscience drug discovery. Nat Rev Drug Discov 2016;15:97-109
53. Desai M, Kahn I, Knoblich U, et al. Mapping brain networks in awake mice using combined optical neural control and fMRI. J Neurophysiol 2011;105:1393-1405
54. Kahn I, Desai M, Knoblich U, et al. Characterization of the functional MRI response temporal linearity via optical control of neocortical pyramidal neurons. J Neurosci 2011;31:15086-15091
55. Abe Y, Sekino M, Terazono Y, et al. Opto-fMRI analysis for exploring the neuronal connectivity of the hippocampal formation in rats. Neurosci Res 2012;74:248-255
56. Li N, van Zijl P, Thakor N, Pelled G. Study of the spatial correlation between neuronal activity and BOLD fMRI responses evoked by sensory and channelrhodopsin-2 stimulation in the rat somatosensory cortex. J Mol Neurosci 2014;53:553-561
57. Christie IN, Wells JA, Southern P, et al. fMRI response to blue light delivery in the naive brain: implications for combined optogenetic fMRI studies. Neuroimage 2013;66:634-641
58. Lebhardt P, Hohenberg CC, Weber-Fahr W, Kelsch W, Sartorius A. Optogenetic fMRI in the mouse hippocampus: Hemodynamic response to brief glutamatergic stimuli. J Cereb Blood Flow Metab 2016;36:629-638
59. Chen Y, Pais-Roldan P, Chen X, Frosz MH, Yu X. MRI-guided robotic arm drives optogenetic fMRI with concurrent Ca(2+) recording. Nat Commun 2019;10:2536
60. Chen X, Sobczak F, Chen Y, et al. Mapping optogenetically-driven single-vessel fMRI with concurrent neuronal calcium recordings in the rat hippocampus. Nat Commun 2019;10:5239
61. Monfaredi R, Cleary K, Sharma K. MRI Robots for Needle-Based Interventions: Systems and Technology. Ann Biomed Eng 2018;46:1479-1497
62. Schwarzmaier HJ, Eickmeyer F, Fiedler VU, Ulrich F. Basic principles of laser induced interstitial thermotherapy in brain tumors. Med Laser Appl 2002;17:147-158
63. Quesson B, de Zwart JA, Moonen CT. Magnetic resonance temperature imaging for guidance of thermotherapy. J Magn Reson Imaging 2000;12:525-533
64. Schwarzmaier HJ, Eickmeyer F, von Tempelhoff W, et al. MR-guided laser irradiation of recurrent glioblastomas. J Magn Reson Imaging 2005;22:799-803
65. Schwarzmaier HJ, Eickmeyer F, von Tempelhoff W, et al. MR-guided laser-induced interstitial thermotherapy of recurrent glioblastoma multiforme: preliminary results in 16 patients. Eur J Radiol 2006;59:208-215
66. Carpentier A, McNichols RJ, Stafford RJ, et al. Real-time magnetic resonance-guided laser thermal therapy for focal metastatic brain tumors. Neurosurgery 2008;63:ONS21-28; discussion ONS28-29
67. Hawasli AH, Bagade S, Shimony JS, Miller-Thomas M, Leuthardt EC. Magnetic resonance imaging-guided focused laser interstitial thermal therapy for intracranial lesions: single-institution series. Neurosurgery 2013;73:1007-1017
68. Jethwa PR, Barrese JC, Gowda A, Shetty A, Danish SF. Magnetic resonance thermometry-guided laser-induced thermal therapy for intracranial neoplasms: initial experience. Neurosurgery 2012;71:133-144; 144-135
69. Candela-Canto S, Alamar M, Alaez C, et al. Highly realistic simulation for robot-assisted hypothalamic hamartoma real-time MRI-guided laser interstitial thermal therapy (LITT). Childs Nerv Syst 2020;36:1131-1142

70. Ginalis EE, Danish SF. Magnetic resonance-guided laser interstitial thermal therapy for brain tumors in geriatric patients. Neurosurg Focus 2020;49:E12
71. Arocho-Quinones EV, Lew SM, Handler MH, et al. Magnetic resonance-guided stereotactic laser ablation therapy for the treatment of pediatric brain tumors: a multiinstitutional retrospective study. J Neurosurg Pediatr 2020:1-9
72. Brown MG, Drees C, Nagae LM, Thompson JA, Ojemann S, Abosch A. Curative and palliative MRI-guided laser ablation for drug-resistant epilepsy. J Neurol Neurosurg Psychiatry 2018;89:425-433
73. Lee EJ, Kalia SK, Hong SH. A Primer on Magnetic Resonance-Guided Laser Interstitial Thermal Therapy for Medically Refractory Epilepsy. J Korean Neurosurg Soc 2019;62:353-360
74. Gupta K, Cabaniss B, Kheder A, et al. Stereotactic MRI-guided laser interstitial thermal therapy for extratemporal lobe epilepsy. Epilepsia 2020;61:1723-1734
75. Gupta K, Dickey AS, Hu R, Faught E, Willie JT. Robot Assisted MRI-Guided LITT of the Anterior, Lateral, and Medial Temporal Lobe for Temporal Lobe Epilepsy. Front Neurol 2020;11:572334
76. Dolmans DE, Fukumura D, Jain RK. Photodynamic therapy for cancer. Nat Rev Cancer 2003;3:380-387
77. Kwiatkowski S, Knap B, Przystupski D, et al. Photodynamic therapy - mechanisms, photosensitizers and combinations. Biomed Pharmacother 2018;106:1098-1107
78. Gross S, Gilead A, Scherz A, Neeman M, Salomon Y. Monitoring photodynamic therapy of solid tumors online by BOLD-contrast MRI. Nat Med 2003;9:1327-1331
79. Leroy HA, Vermandel M, Leroux B, et al. MRI assessment of treatment delivery for interstitial photodynamic therapy of high-grade glioma in a preclinical model. Lasers Surg Med 2018;50:460-468
80. Bechet D, Auger F, Couleaud P, et al. Multifunctional ultrasmall nanoplatforms for vascular-targeted interstitial photodynamic therapy of brain tumors guided by real-time MRI. Nanomedicine 2015;11:657-670
81. Xie W, Guo Z, Gao Q et al. Manganese-doped layered double hydroxide: a biodegradable theranostic nanoplatform with tumor microenvironment response for magnetic resonance imaging-guided photothermal therapy. ACS Appl Bio Mater 2020;3:5845-5855
82. Anwar AR, Muthalib M, Perrey S, et al. Effective Connectivity of Cortical Sensorimotor Networks During Finger Movement Tasks: A Simultaneous fNIRS, fMRI, EEG Study. Brain Topogr 2016;29:645-660
83. Pouliot P, Tremblay J, Robert M, et al. Nonlinear hemodynamic responses in human epilepsy: a multimodal analysis with fNIRS-EEG and fMRI-EEG. J Neurosci Methods 2012;204:326-340
84. D?hne S, Bießmann F, Samek W, et al. Multivariate machine learning methods for fusing multimodal functional neuroimaging data. Proc IEEE 2015;103:1507-1530
85. Abbasi A, Goueytes D, Shulz DE, Ego-Stengel V, Estebanez L. A fast intracortical brain-machine interface with patterned optogenetic feedback. J Neural Eng 2018;15:046011