Magnetic Resonance Imaging (MRI)を用いた動物のイメージング
Introduction to magnetic resonance imaging (MRI) in animals
(Lecture in Japanese)

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Atsushi Yamada (Advanced Medical Research and Development Division, Medical Innovation Research Center)

本講義では，講師がこれまで実施経験のある術前 MRI・術中 CT 画像を用いたイメージレジストレーションや，研究開発してきたリアルタイム MRI 画像誘導手術システムなどを例に，臨床用 MRI を用いた手術やシステム研究を紹介する．また，それらの研究で実施したミニブタを用いた動物実験のプロセスを説明する．

In this lecture, research on navigation systems using clinical MRI is presented, including imaging systems in which the lecturer has been involved. These systems include image registration for liver cryo-ablation, which utilizes preoperative MRI and intraoperative CT images, as well as real-time MRI image-guided navigation systems for microwave liver ablation. The animal experiment using mini pigs employed in these studies was also explained.

Introduction to Magnetic Resonance Imaging (MRI) in Animal Research

Atsushi Yamada, PhD
Specially Appointed Associate Professor
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Medical Innovation Research Center

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Lecturer's basic information

1. Research background

- Robotics and medical engineering
- Development of medical devices and systems

2. Current research interests

- Image-guided therapy and navigation systems
- Translational research using clinical MRI
- Flexible endoscopes, catheters, and surgical devices

3. Perspective for this lecture

- Using clinical MRI as a research platform
- Connecting imaging, animal experiments, and device/system development

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Institutional / Academic Experience

- RIKEN: Research experience in robotics and control
- Shiga University of Medical Science: Faculty / Researcher in medical engineering
- Carnegie Mellon University: Research stay in robotics and medical device development
- Harvard Medical School / Brigham and Women's Hospital: Research stay in image-guided therapy and translational research

Using Clinical MRI as a Research Platform

In this lecture, we will learn the overall research process from MRI fundamentals and hardware to animal experiments, image processing, and image-guided therapy/navigation.

1 MRI Basics

- Principles and features of MRI
- Pulse sequences and imaging methods
- Imaging parameters and coils
- Comparision with other modalities

2 MRI Hardware and Environment

- Types and components of MRI systems
- MRI environment (magnetic field, RF, shielding)
- Safety management and MR compatibility
- Cooling system and quench protection
- Key points for daily use

3 Animal Imaging Workflow

- Overall workflow of animal experiments
- Anesthesia and physiological monitoring
- Preparation of coils and animal beds
- Experimental environment in the MRI room
- Pit-in / Pit-out considerations

4 Image Processing and Analysis

- Handling DICOM data
- Use of 3D Slicer and related tools
- Visualization and quantification
- Data management and sharing

5 Image-Guided Therapy and Navigation Research

- Preoperative MRI and intraoperative CT image registration
- Real-time MRI navigation
- Robot-assisted therapy
- Research case studies using mini-pigs

Learning Goals

- ✓ Understand MRI principles, hardware, and environment, and use MRI safely and effectively for research.
- ✓ Understand the end-to-end workflow of animal experiments and plan and conduct experiments in MRI settings.
- ✓ Understand MRI data analysis methods and leverage research data.
- ✓ Understand image-guided intervention/navigation research and envision future clinical applications.

MRI is a comprehensive platform that supports research and therapy—not just an imaging device.

#1 Magnetic resonance imaging (MRI)

MRI scanners in SUMS

3 T MRI scanner (Verio dot, SIEMENS Healthineers)

Clinical MRI: for patients and medium- to large-sized animals

4.7 T MRI scanner (BioSpec 47/40 USR, Bruker)
https://www.bruker.com/ja/products-and-solutions/preclinical-imaging/mri/biospec/biospec-47-40.html

Research MRI: for small- to medium-sized animals

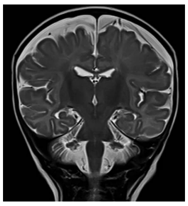
3T MRI Scanner at SUMS

3 T MRI scanner (Verio dot, SIEMENS Healthineers)

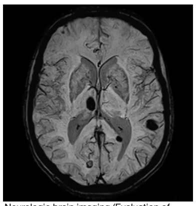
It took more than 7 hours to move the scanner into the room using a crane system (2014).

- Large and heavy: 8,300 kg
- Safety consideration: The MRI scanner continuously generates a magnetic field 365 days a year, even when the system power is turned off.
- Recommendation: Perform scanning with at least two staff members.

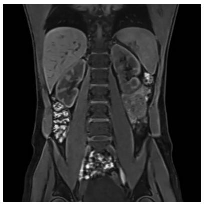
MRI images



Pediatric brain imaging (quick scan and motion compensation)



Neurologic brain imaging (Evaluation of pathology from disc herniation to acute stroke)



Body: Free-breathing high-resolution Magnetic resonance cholangiopancreatography (MRCP)

Verio dot 3T, Siemens Healthineers

https://www.siemens-healthineers.com/en-us/magnetic-resonance-imaging/3t-mri-scanner/magnetom-verio

Imaging Principles

Dr. Paulien Moyaert, How does an MRI works? | MRI basics explained | Animation

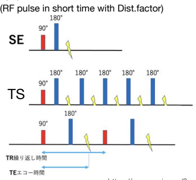
https://www.youtube.com/watch?v=FvOezMIL9BU

Pulse sequence

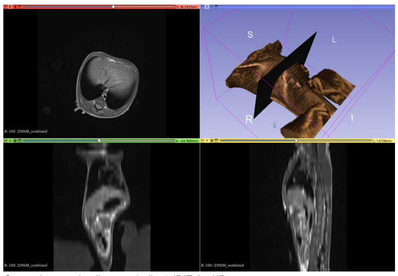
equence information can be obtained from the DICOM header.

tse_9_db_t1_iPAT_fastHR
- tse2d1_9
  - turbo spin echo (basic sequence)
  - 2D
  - contrast:1
  - turbo factor:9 (x9 faster)
  - db (dark blood: suppression of intravascular signal to facilitate detection of arterial plaques)
  - T1-weighted images: fat appears relatively bright; T2-weighted images: water/fluid appears relatively bright.
  - iPAT (parallel imaging with GRAPPA reconstruction)
  - GRAPPA: GeneRalized Autocalibrating Partially Parallel Acquisitions
  - fastHR (RF pulse in short time with Dist.factor)

static magnetic field
RF pulses: 90, 180



https://mrsenpai.com/?p=210



Cynomolgus monkey liver, tse_9_db_t1_iPAT_fastHR

3 steps for MRI scanning

> Select appropriate pulse sequences based on the study objectives.
2D, 3D, TSE, Dixon, etc.

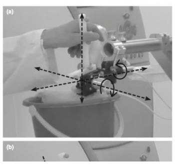
> Optimize sequence parameters and coils for the target animal.
Scanning time, FOV, TR, TE, flip angle, acquisition matrix, slice thickness, etc.

> Establish reproducible protocols for repeated use.

Reporting MRI Scan Parameters in Publications

The MRI sequences and acquisition parameters used in your experiments should be reported in the Materials and Methods section of your paper.

distributed randomly as targets. A convex probe was used for US imaging. The scan phase acquired a T1 weighted three-dimensional (3D) image in the coronal plane with a Spine Matrix Coil using a 3D fast acquisition low flip angle spoiled gradient echo sequence (TR/TE = 8.6/3.86 ms; flip angle = 25°; acquisition matrix = 256 × 256; field of view (FOV) = 240 × 240 mm^2; slice thickness = 2.5 mm). The preset distance was set to 150 mm to avoid contact between the needle guide and phantom surface during path planning. After path planning, the water-filled rubber bag was placed on the phantom surface with the appropriate amount of gel (Aquasonic 100 Ultrasound Transmission Gel, 250 ml, Parker Laboratories, Inc., Fairfield, NJ; Fig. 6). The needle guide was moved along the needle path until the US probe had sufficient contact with the rubber bag, and then a 20 cm 14 gauge MRI-compatible needle (Invivo, Gainesville, FL) with a beveled tip was used. We performed the feasibility study five times and recorded the time required for each setup (Fig. 5).



Yamada A, Tokuda J, Naka S, Murakami K, Tani T, Morikawa S (2020) Magnetic resonance and ultrasound image-guided navigation system using a needle manipulator. ***Med Phys*** *47(3):850–858*

2.2.2.2. MRI. As reported previously [26], the minipigs were first placed in a supine position on the examination table. The abdominal area of the minipigs was scanned using a wide-bore 3 T (T) MRI scanner (Magnetom Verio Dot, Siemens Healthcare, Erlangen, Germany) with a dedicated 4-channel large flex coil. The images were scanned in the transverse plane using 3D T1-weighted gradient-echo 2-point Dixon imaging (TR/TE = 5.26/2.46 ms; flip angle = 10°; acquisition matrix = 352 × 172; field of view (FOV) = 285 × 350 mm^2; slice thickness = 1.0 mm). To acquire each TE image, this Dixon imaging method additionally calculated fat-

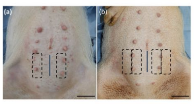


Fig. 2. Areas into which the implant aggregates were inserted. (a) Insertion area in the single group. (b) Insertion area in the double group. The gray line represents the 6-cm incision. The black dotted area shows where the implant aggregates were inserted. Scale bar: 5 cm.

only images. The breath was controlled by intravenous injection of 0.4 mg/kg rocuronium bromide (ESLAX®, MSD K.K., Tokyo, Japan) during scanning. The volume of the implant aggregate and of the newly formed adipose tissue inside the implant aggregate were quantified using 3D Slicer [27], a software package for the analysis of medical images.

Ogino S, Yamada A, et al. (2023) Long term observation of de novo adipogenesis using novel bioabsorbable implants with larger size in a porcine model. ***Regen Ther*** *24:324–331*

#2 MRI scanner

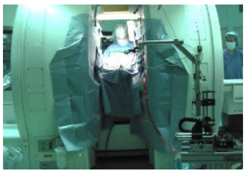
MRI scanner types

Verio dot 3T, Siemens Healthineers
Picture: 3T MRI room, Shiga University of Medical Science

Closed-bore type
3 T

APERTO Lucent Plus, FUJIFILM Corp.
https://www.fujifilm.com/jp/ja/healthcare/mri-and-ct/permanent-magnet-open-mri-system/airis-vento-plus

Horizontal open-bore type
0.4 T

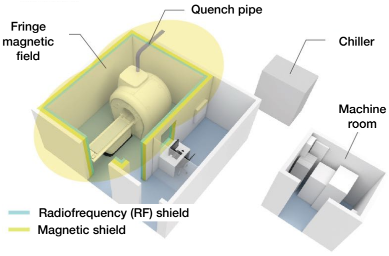


Signa SP/2, GE HealthCare
Picture: Interventional MRI room, Shiga University of Medical Science Hospital

Vertical open-bore type
0.5 T

Scanner room

Superconducting MRI system (<-> permanent-magnet MRI system)



General layout of an MRI scanner room
https://www.fujifilm.com/jp/ja/healthcare/mri-and-ct/permanent-magnet-open-mri-system/aperto-lucent-plus/cost-merit

Magnetic shield
Picture: 3T MRI room (at the time of under construction) in Shiga University of Medical Science

Infrastructure Supporting MRI: Magnet–Helium–Chiller–Quench

MRI operation depends not only on the imaging system itself but also on supporting infrastructure that must operate continuously.

1 Magnet (Superconducting magnet)
- Generates a strong magnetic field using superconducting coils
- The magnetic field is maintained continuously, 365 days a year

2 Helium (Liquid helium)
- Keeps the magnet at cryogenic temperature
- Essential for maintaining superconductivity

3 Cold head / Refrigeration system (Cryogenic / refrigeration system)
- Cooling system that maintains the helium environment

4 Chiller (Cooling water circulation unit)
- Cools the refrigerator / cold head
- Auxiliary equipment supporting stable operation

Quench (Abnormal / emergency event)
- Loss of superconductivity
- Rapid vaporization of liquid helium
- Helium is vented through the quench pipe
- System shutdown and safety management are required

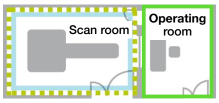
Safety of personnel and appropriate emergency response take top priority.

Dependency relation (Normal operation)
4 Chiller → 3 Cold head / Refrigeration system → 2 Helium → 1 Magnet
The chiller supports the cooling system; the cooling system maintains the helium environment; helium supports the superconducting magnet.

Practical points
- MRI maintains its magnetic field continuously, 365 days a year
- Sound helium and cooling systems are essential for stable operation
- Chiller replacement and helium refilling are important tasks for maintaining the research platform
- Prolonged interruption of the cooling system can lead to helium loss and serious effects on MRI operation

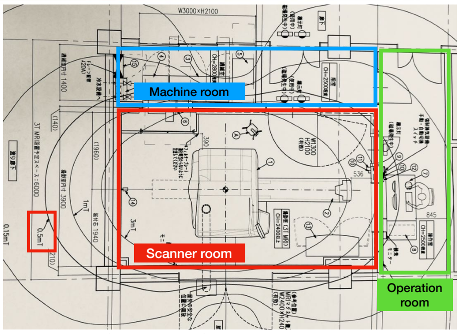
MRI is not simply an imaging device. It is also a research platform sustained by continuous infrastructure operation.

Magnetic field



Radio wave shield
Magnetic shield

- The 5-gauss line (0.5 mT) is a conventional boundary used to indicate an area of low fringe magnetic field.
- The MRI scanner continuously generates a magnetic field 365 days a year, even when the system power is turned off.



Room design: 3T MRI room in Shiga University of Medical Science

Common MRI Safety Hazards

Ferromagnetic objects in the scanner room

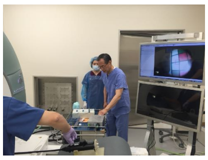
Playing with MRI before quenching 2019
https://www.youtube.com/watch?v=IF6CMrjGNN4&t=26s

Dangers of MRI
https://www.youtube.com/watch?v=plvIEf7JsKo&t=34s

MR-Compatible and MR-Incompatible Equipment

Incompatible
ID cards, bank cards, pens, scissors, staplers, keys, injectors, belts, watches, smartphones, PCs, ECUs, motors, cables, stainless-steel medical instruments, energy devices, etc.

Compatible
Ultrasonic motors and MRI-compatible devices and equipment made from nonmagnetic materials such as aluminum, titanium, copper, brass, and resin.



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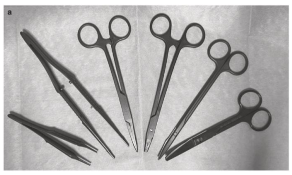
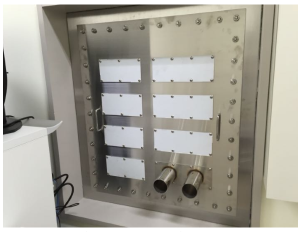


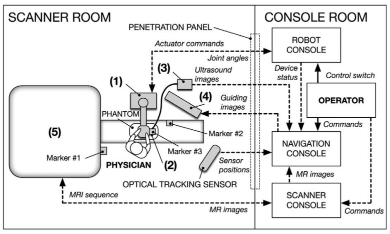
Mekata E, Yamada A, Shimagaki M, Kajiyama T, Tani T (2021) Lightweight Carbon-Reinforced Resin Surgical Instruments. In: Takenoshita S., Yasuhara H. (eds) **Surgery and Operating Room Innovation**. Springer, Singapore.

Penetration panels

Cable access between the scanner room and the control room



Picture: 3T MRI room in Shiga University of Medical Science



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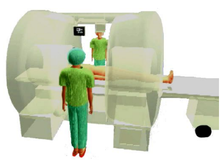
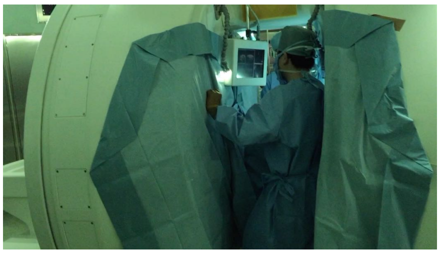
Key Points

- We can perform a wide range of experiments using MR-compatible instruments (energy devices) in the magnet room.
- We can use desktop-class systems in the magnet room provided that they remain outside the 5-gauss line.
- We can operate a ventilator or other equipment located outside the magnet room by routing hoses and cables through the penetration panels.

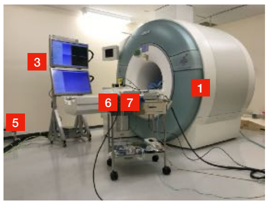
Interventional MRI at SUMS Hospital

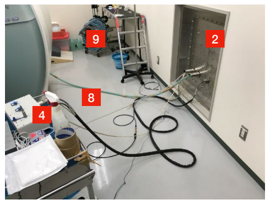




Interventional MRI room, Shiga University of Medical Science Hospital

3T MRI Room at SUMS





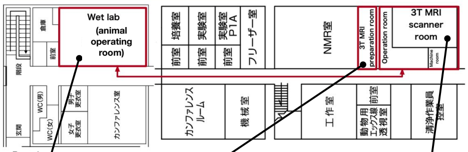
1. 3T MRI scanner
2. Two penetration panels
3. MR-compatible dual monitors for displaying the navigation UI
4. MR-compatible sequence-driven 6-axis magnetic sensors (2 channels)
5. Optical tracking sensor
6. MR-compatible flexible endoscope
7. MR-compatible flexible microwave probe
8. Ventilator
9. MR-compatible robot manipulator
10. Two dehumidifiers

#3 MRI Scanning Workflow for Medium- and Large-Sized Animals

Animal scanning process in SUMS

1. The target animal is transported from RCALS (the SUMS Animal Center).
2. Anesthesia is induced in the wet-lab animal operating room.
3. The anesthetized animal is transported to the 3T MRI room on a plastic bed placed on a metal cart.
4. The animal, together with the plastic bed, is transferred onto the MRI scanner table.
5. The anesthesia machine is placed in the equipment room and connected to the scanner room through the penetration panel.

Rooms for Animal MRI Scanning at SUMS

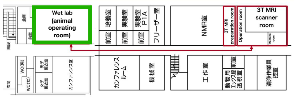


Wet Lab (Animal Operating Room)

3T MRI preparation room

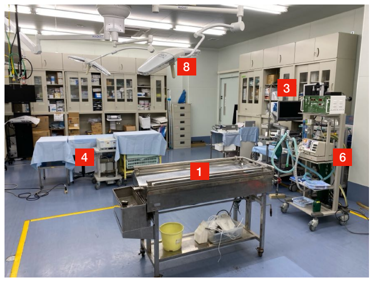
3T MRI room

Wet Lab (Animal Operating Room)



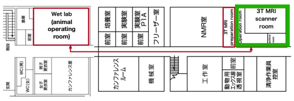
Equipment (selected items)

1. Operating tables for animals
2. MR-compatible resin bed
3. Cardiovascular ultrasound system (Acuson S2000, Siemens Healthcare)
4. Surgical energy devices (Acrosurg microwave scissors, electric scalpels, RF devices)
5. Endoscope systems
6. Ventilator for animals (Compose X, Metran Co., Ltd.)
7. Bedside monitor (BSM-3000, Nihon Kohden Co., Ltd.)
8. Operating lights

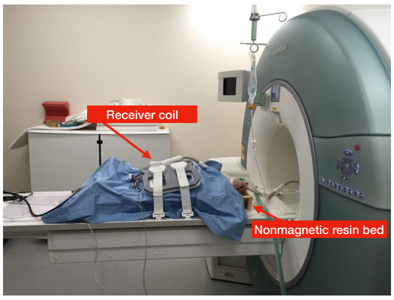


Wet Lab (Animal Operating Room)

3T MRI room

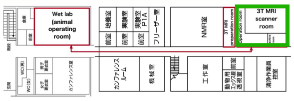


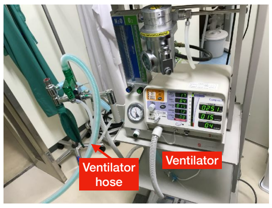
3T MRI control room



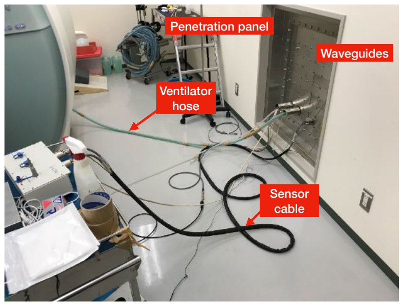
Mini-pig positioned on the scanner table using a nonmagnetic resin bed

3T MRI room



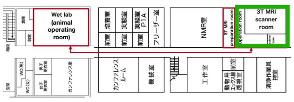


Ventilator in the control room



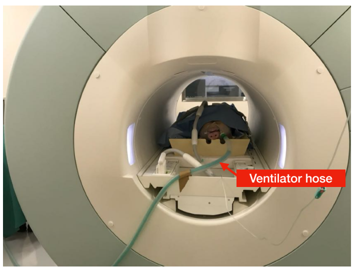
3T MRI scanner room

3T MRI room



3T MRI scanner room

Pit-in/Pit-out scanning

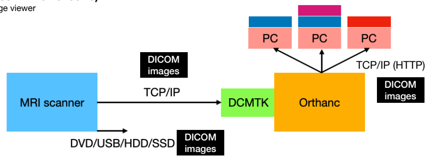


3T MRI scanner room

#4 Image Post-processing

Post-processing software

- **3D Slicer (https://www.slicer.org/)**
  Free, open-source software for visualization, processing, segmentation, registration, and analysis of medical, biomedical, and other 3D images and meshes; and planning and navigation of image-guided procedures.
- **ImageJ (https://imagej.nih.gov/ij/index.html)**
  Image processing and analysis in Java
- **Orthanc (https://www.orthanc-server.com/)**
  Open-source, lightweight DICOM/PACS server
- **DCMTK (https://www.dcmtk.org/en/)**
  A collection of libraries and applications implementing large parts of the DICOM standard.
- **OsiriX (https://www.osirix-viewer.com/)**
  A widely used medical image viewer



3D Slicer

3D Slicer (https://www.slicer.org/)
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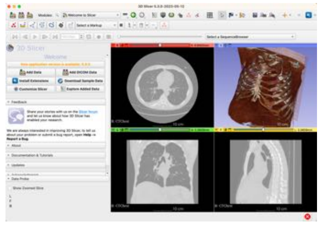
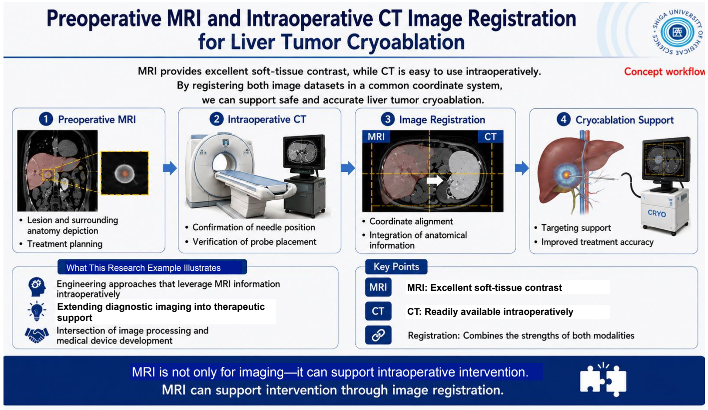


#5 Research examples

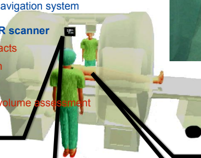


#5-1 Interventional MRI at SUMS Hospital

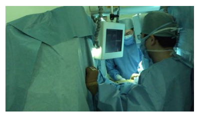
Atsushi Yamada, PhD | Shigeyuki Naka, MD, PhD | Shigehiro Morikawa, MD, PhD | Tohru Tani, MD, PhD

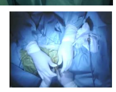
Microwave Needle Ablation

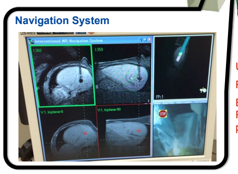
- More than 200 cases of real-time MR-guided liver tumor ablation were performed.
  - Open MRI scanner (Signa SP 0.5T, GE Healthcare)
  - Real-time MR image-guided navigation system



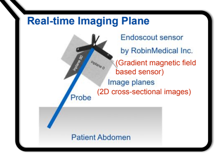
Real-time visualization of needle artifacts
- Actual relative position and depth
- No radiation exposure
- Functional imaging and thermal volume assessment
- Improved safety





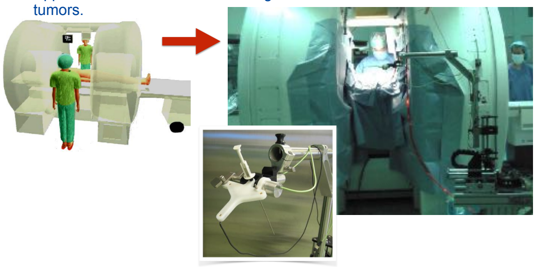


Upper images:
Real-time MRI
Bottom images:
Reconstructed preprocedural MRI



Robot-Assisted Needle Ablation

- A motorized manipulator was used in place of one surgeon for needle guidance.
- The manipulator guided the needle trajectory.
- Applied in 23 clinical cases of MR-guided microwave ablation for liver tumors.

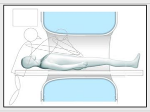


#5-2 Real-time MRI navigation system

Atsushi Yamada, PhD | Shigeyuki Naka, MD, PhD | Shigehiro Morikawa, MD, PhD | Tohru Tani, MD, PhD

Yamada A, Naka S, Dang KT, Morikawa S, Tani T (2020) Development of an MR-Compatible High-Definition Flexible Endoscope for Real-Time MR Image-Guided Microwave Ablation. In: Van Toi V., Le T., Ngo H., Nguyen TH. (eds) 7th International Conference on the Development of Biomedical Engineering in Vietnam (BME7). BME 2018. IFMBE Proceedings, vol 69, 21-26, Springer, Singapore.

Purpose

	GE Signa SP	State-of-the-art
Bore	Open	Closed
Accessibility		
Magnetic Field Strength	0.5 T	3 T
Imaging rate	2 sec/slice	≦2 sec/slice
Availability	Available only at our hospital	Around the world

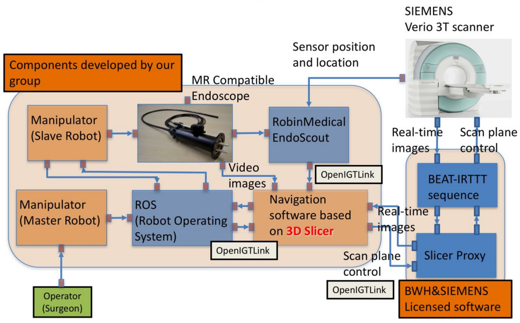
Aim: To develop an access method and navigation system that would translate our real-time MRI system to widely available closed-bore MRI scanners.

Developed System

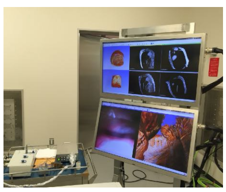
Target Scanner
3T MRI scanner (Siemens Verio Dot, 70-cm wide bore)

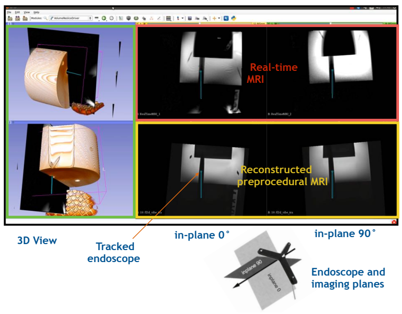
Major Components Developed
1. MR-compatible high-definition (HD) flexible endoscope
2. Real-time MRI sequence
3. Navigation system for dual in-room monitors

System Configuration



Real-Time MR Navigation User Interface



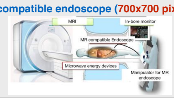


Animal Study

Female pig (body weight: 32 kg)
Team: 4 surgeons and 1 engineering researcher

Conclusion

- Developed an MR-compatible HD endoscope.
- Developed a real-time MR image-guided navigation system dedicated to the endoscope.

	GE Signa SP	Our system
Bore	Open	Closed
Accessibility		MR compatible endoscope (700x700 pixels) 
Magnetic Field Strength	**0.5 T**	**3 T**
Imaging rate	**2 sec/slice**	**0.5 sec/slice**
Availability	Available only at our hospital	Widely available worldwide