the future of drug delivery

angie

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Report on the interface between electromagnetic and angiography systems

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PROJECT DETAILS

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Abstract	This deliverable describes the developed interface between electromagnetic and angiography systems, to allow the use of a angiography system to track the position of the released capsules. Imaging modalities play a crucial role in modern healthcare, allowing for visualization of biological tissue and tracking of objects such as microrobots for drug delivery. Fluorescence imaging, using near-infrared light, has gained popularity due to its non-harmful nature and potential for in vivo tracking of microrobots. Magnetic resonance imaging (MRI) offers high-resolution imaging without ionizing radiation, and can extract 3D position information. Magnetic particle imaging (MPI), a newer modality, tracks superparamagnetic nanoparticles and has potential for tracking microrobots, but human-scale scanners are not yet commercially available. Ultrasound imaging is widely used in clinical settings for its real-time imaging capabilities, but localization can be challenging in the presence of bone. Fluoroscopy, based on X-ray technology, provides real-time and contrast-rich images, but lacks 3D information. Imaging systems for navigation in drug delivery systems should meet requirements such as availability in hospitals, compatibility with an eMNS, contrast-rich imaging, real-time feedback, 3D localization, and non-harmful imaging modalities.
Keywords	Fluoroscope; Interface; Navigation System.

DISSEMINATION LEVEL

PU	Public, to be freely disseminated	X
CO	Confidential, only for members of the consortium (including the Commission Services)	

LIST OF BENEFICIARIES

No.	Participant organisation name	Short name	Country
1.	Swiss Federal Institute of Technology Zürich	ETH	Switzerland
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1. Imaging modalities

1.1. Current state-of-the-art

Nowadays, a wide variety of imaging modalities are available in a hospital. Their size ranges from a tabletop system such as ultrasound (US) device to large magnetic resonance imaging (MRI) devices. Depending on the material properties of the object to be visualized, some imaging modalities are better suited for localization than others. Followingly, some medical imaging techniques will be described.

1.1.1. Fluorescence Imaging

By chemically treating the surface of microparticles, it is possible to localize these with a fluorescence microscope. In recent years this technique has been used increasingly for in vitro experiments with microrobots due to advances in functionalizing the surface of such microrobots.[1] This imaging modality becomes interesting for the biomedical community if the functionalized robots can be visualized by exciting them with a near-infrared (NIR) light source, a region of the electromagnetic spectrum that does not harm the body [2]. Yan et al. demonstrated this technique in an in vivo experiment with mice. They were able to localize microswimmers near the skin. The depth until which particles can be tracked using this method is determined by the penetration depth of the NIR light source, which is usually a few centimeters [3].

1.1.2. Magnetic Resonance Imaging (MRI)

MRI devices have been used since the 1980s for diagnostic purposes of biological tissue. They use a constant magnetic field coupled with radio frequency (RF) pulses and magnetic gradients to visualize objects down to 100 μm. A benefit of this method is the lack of harmful ionizing radiation. Furthermore, different contrast levels can be reached easily by adjusting the frequency of the RF pulses [4]. Despite the magnetic object in the scanned body distorting the acquired image, localization can still be performed by applying some post-processing corrections [5]. Another large benefit of MRI devices is their capability to extract the 3D position of the tracked object. This technique has already been tested by Zhang et al. to visualize helical microswimmers [6].

1.1.3. Magnetic particle imaging (MPI)

MPI is the most recent imaging modality to track magnetic objects in the body. In MPI, superparamagnetic nanoparticles (SPMNPs) are tracked by applying alternating magnetic fields and recording their response to them with the help of pickup coils. Like MRI devices, an MPI scanner uses non-ionizing radiation for localization in 3D. So far, small animals with injected microrobots have been scanned to track the robots. However, the lack of a commercially available human-scale MPI scanner makes further research into tracking robots inside humans difficult [7].

1.1.4. Ultrasound imaging

Ultrasonic waves can penetrate the human body without causing harm. Based on the properties of the tissue with which these waves collide, they will get absorbed, reflected, or scattered. This response can be visualized in real-time with ultrasound (US) imaging devices. They are commonly used in a clinical setting due to their relatively low cost and ease of use [8]. Even though US imaging has been used for tracking magnetic particles, their contrast to the surrounding tissue is low [9]. The frequency of the US wave determines the penetration depth, i.e., the visualized region inside the body. However, if there is a bone between the US source and the target to be tracked, localization is impossible since bones nearly absorb all the US waves [8], [10].

1.1.5. Fluoroscopy

Fluoroscopy is based on X-ray technology that uses ionizing radiation for visualization, i.e., harming the body. A fluoroscope's benefit is its ability to visualize in real-time and its contrast-rich images. Moreover, x-rays can penetrate the skull – which is useful when tracking a magnetic object in the brain. However, a shortcoming of this imaging modality is the loss of 3D information. Additional information is required to extract the 3D position from these images [11].

1.2. Requirements of the imaging system for navigation

The imaging system for navigation is a crucial component of the drug delivery system and allows for position feedback. Therefore, the imaging system should meet the following requirements:

Availability in hospitals: The imaging system should be widely accessible and affordable for hospitals of different sizes and locations. The system should also be easy to install, maintain and operate.
Compatibility with an electromagnetic system (eMNS): The imaging system should be able to interface with an eMNS. The system should support data exchange and synchronization with the eMNS securely and reliably.
Contrast-rich: The imaging system should produce high-quality images that clearly differentiate between different tissues and the delivery system. The system should also allow for the adjustment of contrast levels and image enhancement techniques to suit the preferences and needs of the surgeon.
Real-time: The imaging system should provide real-time feedback to the surgeon during the procedure. The system should have low latency and a high frame rate to ensure smooth and accurate navigation.
3D-localization: The imaging system should enable the 3D-localization of the surgical instruments and the target anatomy. The system should also provide a 3D reconstruction of the surgical field that can be viewed from different angles and perspectives. Tracking algorithms may be implemented to achieve this feature.
Not harmful: The imaging system should not cause any harm or discomfort to the patient or the surgical team. The system should use non-invasive or minimally invasive imaging modalities that do not expose the patient to excessive radiation or heat.

Table 1 the imaging modalities are compared based on the requirement for ANGIE.

	Real-time	Not Harmful	Contrast-rich	3D-localization	Availability in hospitals
Fluorescence	✓	✓	✓	✗	✗
MRI	✗	✓	✓	✓	✓
MPI	✓	✓	✓	✓	✗
US	✓	✓	✗	✗	✓
Fluoroscope	✓	✗	✓	✗	✓

Table 1: Overview of imaging modalities and their properties

In the ANGIE project, we decided to use fluoroscopy as our primary tracking method, because of its ability to produce real-time contrast-rich data, and its availability in hospitals, 3 features of critical importance for the project goals and future uptake of the technology by the health facilities. Therefore, fluoroscopy will be considered in-depth in the following sections.

2. Fluoroscope devices

2.1. Working principle of a fluoroscope

A fluoroscope is a medical imaging device that uses X-rays to produce real-time images of the internal structures of a patient's body. It comprises a fluorescent screen, an X-ray source, and a viewing system.

The working principle of a fluoroscope is as follows:

X-ray Generation: The fluoroscope has an X-ray tube that emits a controlled beam of X-rays. This X-ray beam is directed toward the area of the patient's body that needs to be examined.
X-ray Transmission: The X-ray beam passes through the patient's body, and some of the X-rays are absorbed by the denser tissues, such as bones, while others pass through the less dense tissues, such as muscles and organs.
Detection: Behind the patient's body, there is a fluorescent screen that is sensitive to X-rays. When the X-rays strike the fluorescent screen, they cause it to emit visible light in proportion to the intensity of the X-rays that pass through the patient's body. The emitted visible light from the fluorescent screen is captured by a viewing system, which may consist of an image intensifier or a digital detector. The viewing system converts the visible light into an electronic signal and amplifies it, creating a bright and detailed image in real time.
Modern detectors, also known as flatbed panels (FBPs), are based on individual square detection elements of several hindered square microns. These detectors offer the classical advantages of direct digital image acquisition over conventional fluorescent screens.
Image Formation: The emitted visible light from the fluorescent screen is captured by a viewing system, which may consist of an image intensifier or a digital detector. The viewing system converts the visible light into an electronic signal and amplifies it, creating a bright and detailed image in real time.
Image Display: The amplified electronic signal is then displayed on a monitor or a screen, allowing the radiologist or medical professional to view the real-time images of the internal structures of the patient's body.
Image Interpretation: The radiologist or medical professional can interpret the images in real-time to diagnose various conditions or guide surgical procedures, as they can visualize the movement and function of organs, blood vessels, and other internal structures.

It is important to note that fluoroscopy involves ionizing radiation. Therefore, proper safety measures, including shielding and limiting the duration of exposure, are taken to minimize the risks associated with radiation exposure to the patient and the medical staff.

2.2. Operating modes

A fluoroscope typically has different operational modes that can be selected based on specific imaging needs and requirements. The common operational modes of a fluoroscope include:

Continuous Fluoroscopy: In this mode, the X-ray tube produces a continuous beam of X-rays directed toward the patient's body. The resulting images are displayed in real-time on a monitor.

Continuous fluoroscopy is commonly used for imaging dynamic processes, such as real-time visualization of the movement and function of organs, blood vessels, or joints.

Pulse Fluoroscopy: In this mode, the X-ray tube produces short bursts or pulses of X-rays instead of a continuous beam. The pulses are typically synchronized with the image acquisition system, which captures images during the X-ray pulses. Pulse fluoroscopy can help reduce the overall radiation dose to the patient and the medical staff compared to continuous fluoroscopy, as the X-ray exposure is intermittent.

Digital Subtraction Angiography (DSA): DSA is a specialized mode of fluoroscopy used for imaging blood vessels, particularly in angiography procedures. It involves acquiring images before and after injecting a contrast agent into the blood vessels. Then, the pre-contrast images are subtracted from the post-contrast images to enhance the visibility of the blood vessels and detect any abnormalities, such as blockages or aneurysms.

Roadmapping: Roadmapping is a technique used in interventional procedures, such as catheter-based treatments, where a series of fluoroscopic images are acquired and displayed in real-time to create a roadmap for the medical professional to navigate and guide the catheter or other instruments to the target location.

Digital Radiography: Some modern fluoroscopes may also have a digital radiography mode, which allows for capturing static X-ray images in addition to real-time fluoroscopic imaging. Digital radiography mode can be useful for capturing high-resolution static images for detailed anatomical evaluation or for comparison with previous images.

The specific operational modes available on a fluoroscope may vary depending on the make and model of the equipment, as well as the imaging capabilities and features offered by the manufacturer. Therefore, it is important to use fluoroscopic equipment in accordance with the manufacturer's instructions and relevant safety guidelines and under the supervision of trained medical professionals.

3. Image acquisition and processing

Integrating eMNS with fluoroscopy can enhance the accuracy and safety of procedures, allowing for precise instrument placement and improved patient outcomes. However, there are challenges in interfacing EMNS with fluoroscopes, particularly when obtaining raw images from fluoroscope manufacturers' APIs.

One of the challenges in integrating eMNS with fluoroscopes is obtaining access to the raw images from the fluoroscope's API. Ideally, raw images directly from the fluoroscope would be preferred, as they provide the most accurate and high-quality imaging data for navigation and guidance. However, many fluoroscope manufacturers may not offer APIs that allow direct access to raw images, or the APIs may be proprietary and require specific permissions or agreements for access. This can limit the flexibility and independence of eMNS integration, as the navigation system may rely on processed or screen-captured images, which may have limitations in terms of image quality, resolution, and real-time updates.

To overcome the challenges of obtaining raw images from fluoroscope manufacturers' APIs, an alternative approach is implementing a "screen capture" method and developing custom post-processing algorithms to extract the information from the captured image. In this approach, the eMNS can capture the fluoroscopic images from the display screen of the fluoroscope in real time and then use custom algorithms to process and extract relevant information for navigation and guidance. This approach is applicable regardless of the fluoroscope manufacturer and uses raw images that are as close to the original fluoroscopic images as possible.

Implementing a screen capture approach and developing custom post-processing algorithms comes with its own challenges. One challenge is the potential image quality and resolution loss due to the screen capture process. In addition, the captured images may be affected by the display settings, screen resolution, and other factors. This can impact the accuracy and reliability of the navigation system, as the processed images may not accurately represent the true anatomical structures or instrument positions.

Another challenge is the need for robust and efficient post-processing algorithms that can accurately extract relevant information from the captured images. In addition, custom algorithms may need to be developed to account for the specific characteristics of fluoroscopic images, such as image noise, contrast, and geometric distortions. Finally, the algorithms should also be designed to operate in real-time, as image processing delays can impact the navigation system's real-time guidance.

Despite these challenges, integrating eMNS with fluoroscopes using screen capture and custom post-processing algorithms offers significant advantages in terms of flexibility and independence from fluoroscope manufacturers. It can provide access to imaging data that can be tailored to the specific needs of the navigation system and the medical procedure. However, careful validation and verification of the integrated system's accuracy and safety are essential to ensure accurate navigation and guidance during operations.

In conclusion, integrating eMNS with fluoroscopes presents challenges in obtaining raw images from fluoroscope manufacturers' APIs. Implementing a screen capture approach and developing custom post-processing algorithms can offer an alternative solution to overcome these challenges, providing independence from the manufacturer and access to raw imaging data. However, carefully considering image quality, resolution, and real-time processing is necessary to ensure accurate and reliable navigation and guidance during medical procedures. Further research and development in this area can contribute to improving the seamless integration of EMNS with fluoroscopes, enhancing the precision and safety of image-guided interventions.

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