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Intra-operative Multi-Spectral Imaging Systems for Radical Tumor Resection (MUSIS)

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**Background**
Due to increased knowledge and the introduction of new technologies, the treatment of cancer has made great progress in the last 25 years. In particular, new anti-cancer drugs, treatment regimens, medical imaging technologies and surgical operating techniques have improved life expectancy and quality of life for cancer patients.

Using non-invasive imaging technologies such as CT, MRI and PET, cancer can be detected much earlier and tumors removed either by open surgery or minimally-invasive techniques such as endoscopy or laparoscopy. During such operations, it is of paramount importance that tumors are removed completely (radically) with sufficient tumor-free margin. However, clinical discrimination between tumor and normal tissue remains difficult during an operation. It is therefore difficult to determine an adequate tumor-free margin, making non-radical resection (resections in which the resection margin still contains tumor cells) a serious clinical problem. The identification of lymph node metastases also remains problematic during an operation.

If intra-operative imaging of tumor-free margins and local (lymph node) metastases were possible so that they could be radically removed, the life expectancy of cancer patients could be greatly improved. A promising development in this area is the use of near-infrared fluorescence (NIRF) imaging, in which fluorescent molecules are coupled to proteins (antibodies) or drug molecules that specifically bind to tumor tissue (so-called 'probes'), making real-time visualization of tumor tissue during an operation possible. Tumor cells in the cutting zone between tumor and healthy tissue, or in lymph nodes, could thus be made visible with a high degree of precision and sensitivity.

**Aim**
The aim of the MUSIS project is to develop new technologies that will enable rapid implementation of intra-operative NIRF imaging of tumor tissue in surgical oncology in order to facilitate radical removal of tumor tissue and local (lymph node) metastases while leaving normal tissue intact, thereby increasing life expectancy and quality of life for cancer patients.

**Plan of investigation**
To achieve our aim, we need (new) tumor-specific NIRF probes that can be used in patients, plus NIRF camera systems that are capable of detecting these probes during an operation.

NIRF Probes
At the moment, only two NIRF probes are available that can be used to detect the sentinel lymph node: Methylene Blue (MB) and Indo-Cyanine Green (ICG). The sentinel lymph node is the lymph node into which lymphatic fluid from the tumor drains and in which tumor cells will first metastasize. There are several other NIRF probes produced by MUSIS project partner VisEn Medical (a world leader the field) that will soon move into clinical practice. In addition to these probes, the MUSIS consortium will develop new tumor-directed NIRF probes for tumor detection during surgical operations. These will largely be based on existing tumor-directed antibodies or drugs that recognize up-regulated tumor receptors or membrane markers to which a non-toxic NIRF dye will be coupled. The project will also aim to enhance the NIRF signal using very small (nano-) gold particles coupled to the NIRF probe.

NIRF camera systems
In addition to new NIRF probes, it is essential that good camera systems are developed that can detect NIRF signals with high sensitivity and precision. The MUSIS project will use the world's first real-time multi-spectral NIRF camera system, the Artemis, developed by MUSIS project partner O2view. The use of multi-spectral NIRF imaging has several important advantages, such as filtering out background fluorescence signals and the ability to use multiple NIRF probes at the same time. The project will aim to optimize the Artemis system for intra-operative use in the clinic using the previously mentioned tumor-specific NIRF probes. Furthermore, the project will also develop a new multi-spectral endoscopic/laparoscopic camera system for clinical use.

**Expected results**
Because we can rapidly start on clinical implementation, the expectation is that this technology-based project will lead to a revolution in surgical oncology. It could make it possible for surgeons to be optically guided during surgery to tumor tissue locations with great precision in order to resect tumors with adequate tumor-free margins. The result could be significantly increased life expectancy for cancer patients.