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Chirurgie guidée par fluorescence Techniques d'imagerie d'aide opératoire

Fluorescence Guided Surgery – Intraoperative Imaging Techniques to Support the Physician

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Résumé

La fluorescence est un phénomène physique connu depuis longtemps qui est entré relativement récemment en chirurgie endoscopique. La fluorescence est générée en illuminant certains matériaux avec une lumière d'une couleur spécifique entraînant la génération d'une lumière de couleur différente. Dans la plupart des cas, la couleur a une longueur d'onde plus élevée ; par exemple en utilisant une lumière bleue, il en résulte un signal fluorescent vert ou rouge.
L'usage de la fluorescence facilite une détection plus aisée de tumeur ou une meilleure appréciation des marges tumorales pendant la chirurgie ou permet une évaluation fonctionnelle en temps réel. Ceci peut aider à obtenir une meilleure issue au traitement du patient.
La technologie de l'imagerie aidée par fluorescence fait face à certains défis. L'un de ces défis est en rapport avec la disponibilité de marqueurs de fluorescence appropriés et sûrs, qui puissent être administrés aux patients. En pratique, seuls très peu de ces marqueurs sont disponibles, en particuliers approuvés par les autorités de régulation ; d'autres sont en cours de développement. Les marqueurs en développement sont considérés comme des produits pharmaceutiques avec une procédure lente de développement et d'approbation.
Un autre élément est lié à un équipement chirurgical convenable pour que les systèmes d'imagerie puissent être modifiés de telle façon qu'ils puissent être capables d'être utilisés, à la fois avec la lumière blanche, aussi bien qu'avec l'imagerie fluorescente, sans trop altérer le travail chirurgical ou avoir un impact négatif sur la qualité de l'imagerie de haute définition qui est considérée actuellement comme le standard. Il y a un défi supplémentaire en rapport avec les propriétés physiques de ces marqueurs de fluorescence. La caméra, le système lumineux et les endoscopes doivent être adaptés pour permettre l'utilisation avec les différents marqueurs.
L'imagerie de fluorescence est une technologie intéressante avec un grand potentiel pour une imagerie en temps réel durant la chirurgie endoscopique.

Mots clés

- Fluorescence
- Imagerie
- Laparoscopie
- Vert d'indocyanine
- Diagnostic photo dynamique
- Auto fluorescence
- Perfusion

Abstract

Fluorescence is a long known physical phenomenon which has relatively recently entered endoscopic surgery. Fluorescence is generated by illuminating certain material with light of a specific colour resulting in the generation of light with a different colour. In most cases the colour has a longer wavelength; e.g. applying blue light can result in a green or red fluorescence signal.
Use of fluorescence facilitates an easier detection of tumours or a better delineation of tumour margins during surgery or enables functional assessment in real-time. This will help to achieve a better outcome of patient treatment.
The technology of fluorescence aided imaging is facing some challenges. One of these challenges is related to the availability of suitable and safe fluorescence markers which can be administered to patients. Currently, only very few of these markers are available, i.e. approved by regulatory authorities; others are under development. Fluorescence markers are regarded as pharmaceuticals resulting in a lengthy development and approval process.
Another element is related to the suitable surgical equipment, i.e. the imaging systems have to be modified in such a way that they are capable to be used for both white light as well as fluorescent imaging without impairing the surgical workflow too much or having a negative impact on the high definition imaging quality which is regarded today as a standard.
There is an additionally challenge related to the different physical properties of the fluorescence markers. Camera, light system and endoscopes have to be adapted to allow the use with the different markers.
Fluorescence imaging is an interesting technology with a great potential for real-time imaging during endoscopic surgery.

Keywords

- Fluorescence
- Imaging
- Laparoscopy
- ICG
- PDD
- Autofluorescence
- Perfusion

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Fluorescence is a long known physical phenomenon that is becoming increasingly important in surgery as it offers the possibility to detect and identify structures in real-time which are not visible under ordinary white light. Through the various target applications, ease of use and simple implementation in the operating theater, surgeon technique and clinical outcomes are improving through widespread global use. To address surgeon demand KARL STORZ has provided three fluorescence imaging systems.

Method

Fluorescence imaging is based on the property of certain molecules to emit light after exposure with light of particular wavelength. Fluorophores can be classified into two groups: endogenous and exogenous fluorophores. Endogenous fluorophores are for example structural proteins, porphyrins, lipids and vitamins. Exogenous fluorophores are cyanine dye, photosensitizer or molecular markers, e.g. GFP (green fluorescent protein).
The main challenge is that scattered light from the light source must be filtered out by wavelength-specific optical filters, before reaching the camera head. During open surgery ambient light must also be suppressed.
The technology for fluorescence imaging is facing some challenges. On the one hand the availability of suitable and safe fluorescence dyes (exogenous fluorophores) which can be administered to patients. Currently only very few of these substances are available, i.e. approved by regulatory authorities, others are still under development. On the other hand, the suitable surgical equipment, i.e. the fluorescence imaging systems have to be modified in such a way that they are capable to be used for white light as well as fluorescence imaging, without impairing the surgical workflow too much or having negative impact on the high definition image quality. The technical equipment has to be adapted to allow the use with different fluorescent markers.
KARL STORZ offers three fluorescence imaging solutions. In addition to autofluorescence (AF) and photodynamic diagnosis (PDD) for the visible light spectrum, our key focus is on near infrared imaging (NIR) used in combination with Indocyanine Green (ICG).
Photodynamic diagnostic allows detection of abnormal cell changes at an early stage. A common application for photodynamic diagnosis is in the early detection of non-muscle invasive carcinoma of the bladder, such as carcinoma in situ or papillary tumors. On top of that PDD is used for detection of tumor margins in malignant gliomas.
The principle is based on the characteristics altered metabolic activity found in malignant cells which results in the accumulation of 5-ALA (5 amino levulinic acid) metabolic products. 5-ALA is an intracellular intermediate in the heme biosynthesis process, excess concentrations of 5-ALA leads to an increased accumulation of fluorescent protoporphyrine IX in tumor cells. To achieve the detection of early malignant changes compared to healthy tissue the PDD endoscopic system transmits blue light into the body. The method then exploits the altered metabolism of malignant cells in such a way that tumor cells are optically enriched with the fluorescent molecule protoporphyrine IX. Abnormal cells are precisely distinguished through their typical pink/red coloring relative to the blue healthy surrounding tissue.
Another fluorescence guided surgery imaging technique is the use of autofluorescence (AF). AF enables visualization of tumorous tissue without the use of drugs. As the name implies the technique is based on a group of fluorescent biological molecules naturally occurring in tissue. Proteins like, NADH (nicotinamide adenine dinucleotide), FAD (flavin adenine dinucleotide), collagen or elastin exhibit a unique fluorescence when illuminated with light of a specific wavelength. This autofluorescence occurs mainly in sub-mucosal layers and is importantly shielded by tumors which are arising from the mucosal layer. This enables the differentiation of a tumor as non-fluorescent areas amongst the surrounding fluorescent tissue. The typical application for AF imaging is to detect squamous cell carcinoma of oral or laryngeal or lung tissue and early malignant changes – the key application of AF is the detection of lung cancer.
Near infrared fluorescence in combination with ICG is starting to make significant inroads in surgery. The success of NIR fluorescence is the ability to anatomically mapping up to 10 mm below the tissue surface in real time, which cannot be achieved under ordinary white light. ICG has been in clinical use for a long time. Its first FDA approval in 1959 was approved for liver and heart function testing. ICG is injected intravenously. Besides liver and cardiac function tests ICG is a blood marker used for vascular perfusion control assessment. ICG binds to blood plasma proteins such as albumin and due to combined molecular size remains in the bloodstream (1). ICG is eliminated from the body via the hepatobiliary pathway where it is stored into the gall bladder and finally released into the duodenum.
The advantage of ICG is that its absorption and emission are focused in the near infrared window of tissue, where the absorption due to hemoglobin is much lower than in the ultraviolet and visible spectra. The absorption peak of ICG in water is around ~780 nm and its emission peak around ~ 810 nm.
NIR/ICG imaging is used in minimal invasive and open surgery to detect blood vessels, vascular anomalies, vascular ischemia (perfusion assessment of colorectal anastomosis), and bile flow as well as biliary tree mapping in cholecystectomy surgery (2, 3, 4). In addition, ICG is used in countless studies to visualize the local lymphatic system around a tumor (5).
The solution by KARL STORZ for NIR/ICG imaging consists of the camera control unit IMAGE1 S with full HD image quality, a 3-chip full HD camera head with NIR light sensitivity, the NIR optics for optimal fluorescence excitation and detection as well as the xenon-based D-Light P light source. Light source configuration provides optimal contrast enhancement and fluorescence with background illumination in parallel. Transition between the standard white light visualization and fluorescence mode can be conducted easily using a foot switch.

Conclusion

Technical considerations as well as the behavior of different fluorophores have to be taken into account to exploit the full potential of fluorescence imaging. Fluorescence guided surgery will help to achieve a better outcome of patient treatment with a great potential for real-time imaging.
In result the surgeon can use fluorescence imaging in minimal invasive and open surgery depending on the fluorescent agent for perfusion assessment of anastomotic areas or transplants, vascular anomalies, as well as bile flow, bile leakage and the morphology of the hepatobiliary duct tree or by using 5-ALA products the detection of bladder cancer or visualization and

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detection of tumor margins during glioblastoma surgery. Therefore, KARL STORZ offers an optimal solution for endoscopic and open fluorescence guided surgery with its OPAL1™ technologies.

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