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# Diagnostics and Treatment of Tumours using Laser Techniques

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**Abstract:** Laser spectroscopy techniques can be used for tumour detection as well as for localised therapy of malignancies. Laser-induced fluorescence with or without exogenously administered tumour seeking agents is a promising technique for real-time detection of atypical cells and dysplasia before the diseased areas can be visualised by the naked eye. Tumour borders can also be delineated towards normal non-affected tissue with the same technique. Gas in scattering media absorption spectroscopy can be used for monitoring gas contents in hollow organs in the human body, such as the sinuses in the facial area. Photodynamic therapy utilising red laser light and photosensitising agents is a selective treatment modality for certain types of thin malignancies. By using optical fibres inserted into the tumour mass deep lying tumours can also be treated.

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## 1. Laser induced fluorescence for tumour detection

The most important prognostic factor for cancer patients is early tumour discovery. If malignant tumours are detected during the early non-invasive stage, most tumours show a high cure rate of more than 90 %. If detected in a late stage, the success rate is often very low. There is a variety of diagnostic procedures to be used when a patient has a suspicious tumour. The most common is conventional x-ray imaging. More advanced results are given in computerised investigations, such as CT (computerised tomography) scanning and MRI (magnetic resonance imaging). For certain types of tumours scintigraphic techniques are of great value. Recently, PET (positron emission tomography) scanning has been introduced as a complementary modality, in particular for patients with head and neck cancer. A limiting factor is tumour size and, by definition, and not necessary logical, lymph nodes with a diameter smaller than 1 cm are defined as benign. For many organs visual inspection is performed, either with a magnification unit, such as in the female genital tract or for the hollow organs, with various endoscopes with high quality optics. The epithelium outlining all these organs is the starting site for most malignancies. However, there is a clinical dilemma in differentiating early cancer or precancer from other types of diseases, such as inflammation, infection or chronic irritation of other genesis. The visual characteristics may be the same whether it is a precancer, an early non-invasive malignancy or only benign proliferation. Laser-induced fluorescence (LIF) for tissue characterisation is a technique that can be used for monitoring the biomolecular changes in tissue under transformation from normal to dysplastic and cancerous tissue. It has been shown that these changes appear early in the biological process, before structural tissue changes are seen at a later stage. The technique is based on UV or near-UV illumination of biological tissue for excitation of fluorescence. The fluorescence from the endogenous tissue chromophores alone, or enhanced by exogenously administered tumour seeking substances can be utilised. The technique is non-invasive and gives the results in real-time. LIF can be applied for point monitoring or in an imaging mode for larger areas, such as the vocal cords or the portio of the cervical area.

## 2. Clinical monitoring

Various tumours and also precancerous conditions were monitored by laser-induced fluorescence (LIF). The technique is non-invasive and gives the result in real-time as it relies on optical rather than on histopathological investigation [1]. An example from a patient with a precancerous area is shown in point-monitoring mode (Figure 1). The excitation of the fluorescence was induced by a nitrogen laser (337 nm) pumping a dye laser (405 nm). Two peaks (marked A and B) are seen in the fluorescence spectra. The one at approximately 470 nm represents the endogenous fluorescence from the tissue itself, the autofluorescence, and is a composite from various fluorophores, such as the coenzymes NADH/NAD<sup>+</sup>, elastin, collagen and others. The A peak at 635 nm represents the exogenously administered sensitizer, in this case  $\delta$ -aminolevulinic acid-induced Protoporphyrin IX, which is selectively retained in the precancerous area. As can be seen in the figure the intensity of the B peak decreases in the diseased area at the same time as the A peak increases and a tumour enhanced demarcation is

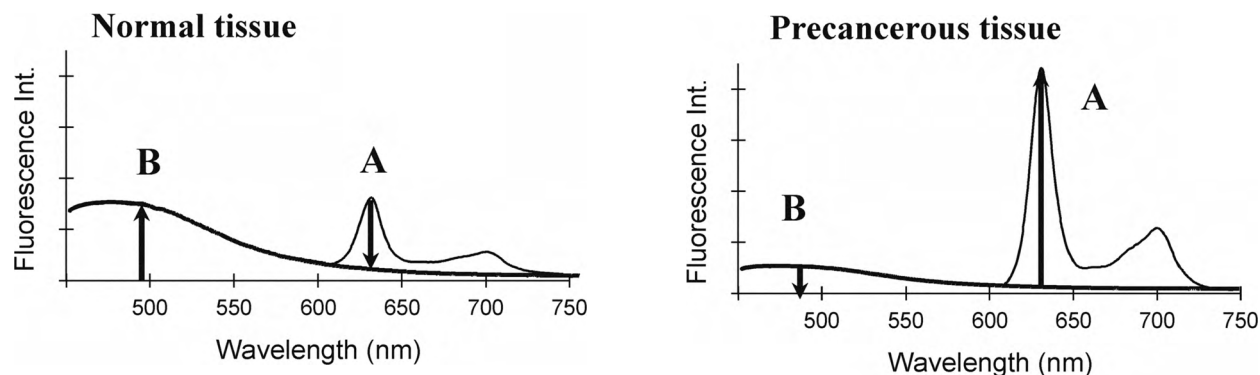


Figure 1. Laser-induced fluorescence spectra for normal oral cavity mucosa and a precancerous lesion on the vocal cord in a patient to whom per oral  $\delta$ -aminolevulinic acid (ALA) was administered. The B peak, represents the endogenous fluorescence and the A peak the ALA-induced Porphyrin IX (PpIX) intensity. The B peak decreases in the precancerous area at the same time as the PpIX-peak (A) increases and by forming the ratio  $A/B$  an enhanced tumour demarcation is achieved.

achieved by forming the ratio  $A/B$ . This ratio is dimensionless and therefore insensitive to distance variations between the probe and the tissue, which is expected when the patient is, e.g., breathing during the examination. Furthermore, the ratio is also immune to topographical formations of the tumour as well as to variations in the technical equipment. Based on the fact that the tissue can be characterised by few interesting structures in the fluorescence spectra tissue imaging can also be performed [2-4]. By building up a catalogue of various diseases in terms of tissue optical characteristics tumour demarcation algorithms can be developed [5,6]. As the LIF technique also can be used for demarcation of malignancies it is a valuable tool for defining the treatment target area and as the sensitising agent is the same for tumour marking as for the tissue sensitisation in photodynamic therapy the two techniques can be combined in a powerful way [3,4].

### 3. Gas in scattering media absorption spectroscopy

Gas Absorption Spectroscopy in Scattering Media (GASMAS) is a non-intrusive technique for examination of the quantity of a certain gas molecule utilising the spectral absorption lines of that particular gas. By using the GASMAS technique the content of, e.g., oxygen and water vapour can be monitored in the air-filled cavities, the sinuses, in the human facial skeleton [7,8]. Also the ventilation between the nasal cavity and the sinuses can be investigated by the same technique. An example from a pilot study is shown in Figure 2.

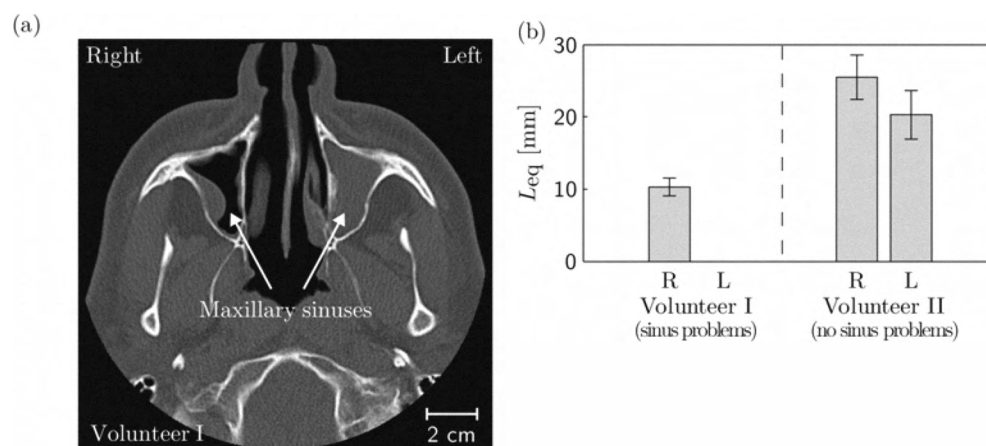


Figure 2. a) A transverse CT image of a volunteer patient with constantly recurring sinus problems preferably from the left maxillary sinus, which is seen with swollen mucosa. b). Comparison between this patient and a healthy volunteer with no sinus problems. The equivalent path for the light,  $L_{eq}$  (mm), calculated from the free oxygen signal reflects the different biological situation for the right and left sinuses in the two subjects investigated.

Fully developed the GASMAS technique might replace investigations based on ionising radiation, such as CT-scanning or radioactive Xenon clearance measurements for ventilation studies of patients with sinus cavity related problems.

#### 4. Photodynamic therapy of malignant tumours

Photodynamic therapy (PDT) is a selective tumour treatment modality for local eradication of tumours, where tumour-seeking substances, such as porphyrins, chlorines and phthalocyanines are employed in combination with red/near-IR laser light to bring about a selective release of toxic singlet oxygen and free radicals in the malignant tumour cells. The use of the haem precursor ALA for tumour selective induction of the photodynamically very active substance Pp IX opens up wide applications for the treatment of various malignancies [9], such as tumours in the skin, on the vocal cords or in the bronchus. A new sensitiser for topical use, based on Temoporfin, has been developed and the first clinical PDT results have recently been published [10].

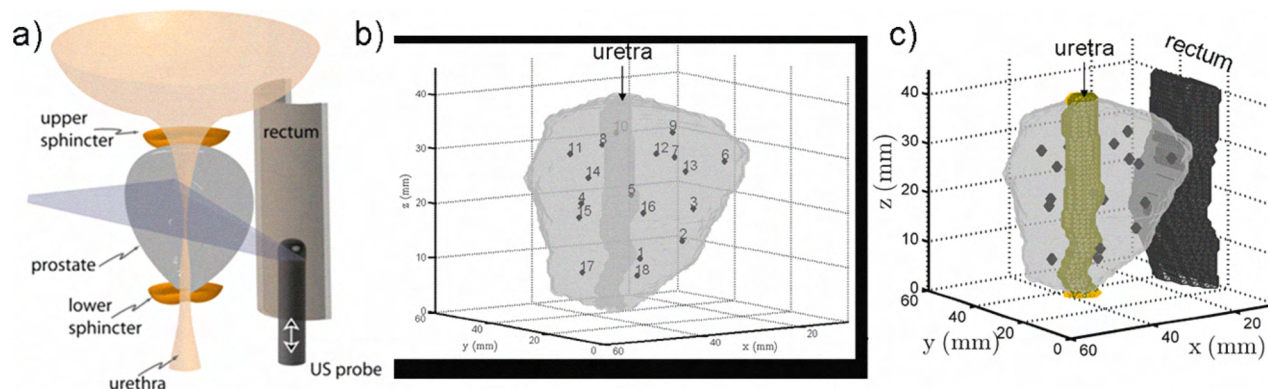


Figure 2. a) Schematic drawing of the human prostate with organs at risk, the upper and lower sphincter, urethra and the rectal intestine. With the ultrasound probe in the rectum a 3-D image of the treatment target can be built-up, b) the positions of the 18 optical fibres for optimal light delivery taken into account the c) position of the urethra and the rectal wall.

Interstitial PDT with fibres inserted into the tumour mass widens up the indications to deeper tumours [11]. An interactive treatment system for feed-back dosimetry calculations during the treatment course has been developed and the first clinical use of this system has started in a Phase I clinical trial.

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