Fiber Optic Probes for Tissue Illumination in Photodynamic Diagnosis (PDD) and Therapy (PDT)

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ABSTRACT

Photodynamic diagnosis (PDD) and therapy (PDT) require light application devices which enable homogeneous illumination of tissue in hollow organs. Three techniques based on modification of the aperture of single fibers are presented mainly for use in urology and pneumology in combination with rigid and flexible endoscopes. All illumination systems allow for nearly entire illumination of the endoscope's viewing field.

A microlens system is used for fluorescence diagnostic purposes in the lung. The system, consisting of two plano convex lenses in a condensor configuration, is attached directly to the fiber. The beam profile is optimized by ray tracing calculations.

For fluorescence excitation of the tumormarker Photofrin II in the urinary bladder a 500 μm-plastic fiber is used. The tip of the fiber is polished to a double cone with angles of 12° and 7°. With this modification the aperture is increased by a factor of two.

Photodynamic treatment of confined superficial tumors in the lung was successfully performed with a fused silica fiber coupled to the endoscope in a special adaptive device. In this procedure laserlight at 630 nm is guided through the optics channel of rigid endoscopes. A homogeneous circular illumination pattern is obtained following exactly the deflection angle of the endoscope.

1. INTRODUCTION

Both photodynamic diagnosis (PDD) and photodynamic therapy (PDT) are based on light induced processes in photosensitized tissue, following absorption of preferentially laserlight in the visible spectral range. In both cases most success is obtained if light is delivered by single flexible fibers coupled to optical diffusers. Dependent on the organ system to be treated, spherical, cylindrical or flat cut fiber optic probes are used (1,2). Due to limitations of the instrumentation channels of the endoscopes the diameter of the modified fiber tips are confined to dimensions below 3 mm.

The three fiber optic probes presented are specially suited for circular homogeneous irradiation of flat tissue surfaces with high aperture. The systems are designed mainly for endoscopic use in the bladder and the lung.

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2. LIGHT APPLICATION SYSTEMS

2.1 Fiberoptic microlens probe

Fig. 1 shows the scheme of the fiberoptic microlens probe and its beam profile . It consists of two plano convex lenses in a condensor configuration. The distance between the lenses with diameters of 0.8 mm is about 0.2 mm. Contrary to a recently published microlens system (3), the fiber is in direct contact with the plane end of the backplaced lens. With a 600 μm fused silica fiber this fiberoptic probe enables homogeneous irradiation of a circular area within a full angle 2 of about 60°.

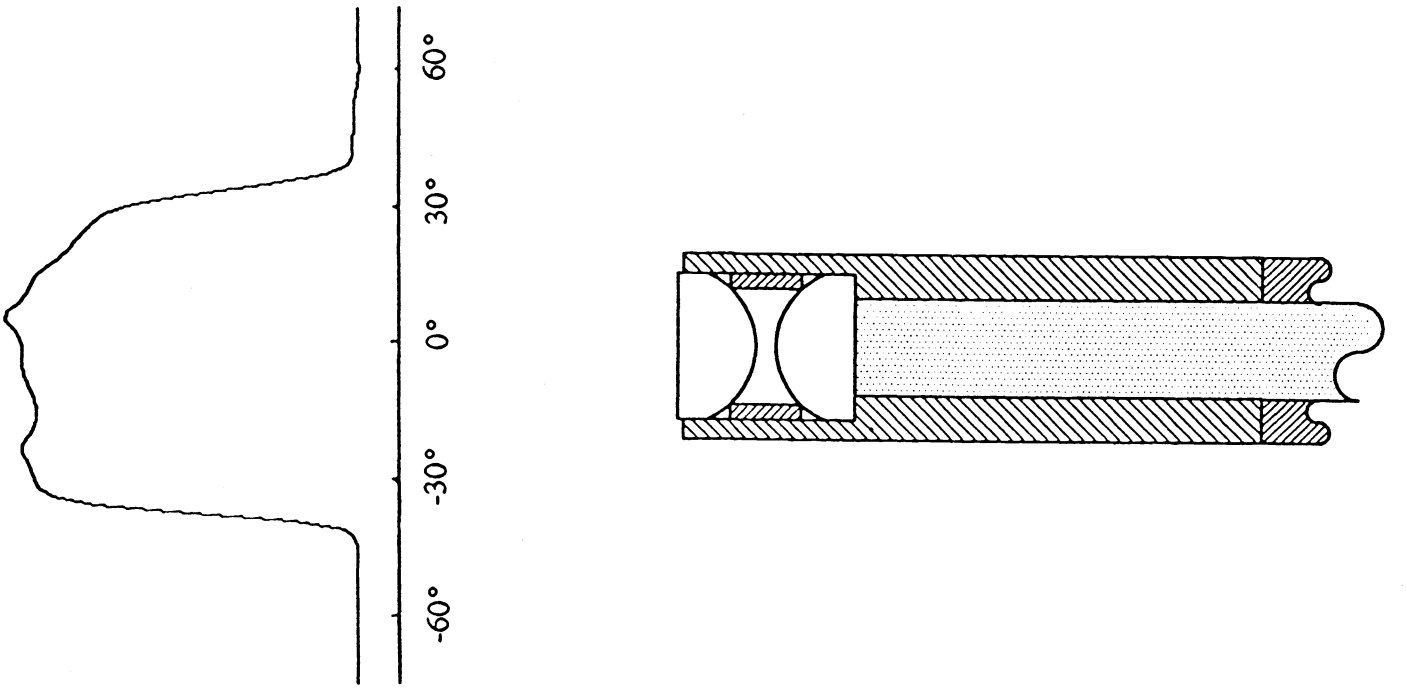

Fig.1 The fiberoptic microlens probe and its beamprofile.

Ray tracing calculations show that homogeneity of the beam profile as well as keeping the illuminated area at a constant distance depends strongly on the ratio of the diameter of the fiber and the lenses. In addition the distance between the lenses and between lens system and plane fiber end influences the optical properties mentioned above. Therefore the arrangement of the system components of lenses and fibers reveals a compromise in the requirements for light application in PDD and PDT.

Compared to a single lens system usually used in Phase III clinical studies for local treatment of lung cancer the angle is enlarged by a factor of nearly 3.

The outer diameter of the stainless steel tube fixing the microlenses and the fiber is reduced to 1 mm which up to now is the smallest lens probe prepared for PDT applications.

The fiber tip, with a transmittance of laserlight at violet, blue and red wavelengths of about 70%, is specially suited for PDD applications. In this case it is preferential to have an overlap of the endoscope's aperture and the illuminated area for fluorescence excitation. On the other hand, the mircolens probe can be used for photodynamic treatment of large areas, e.g. of cancer in the bronchi, where the distance between fiber and tissue surface is often limited.

2.1 Biconic plastic fiber tip

A modified 500 μm plastic fiber is used for fluorescence excitation of Photofrin II in bladder tumor patients. According to Fig. 2 its tip is of biconic shape.

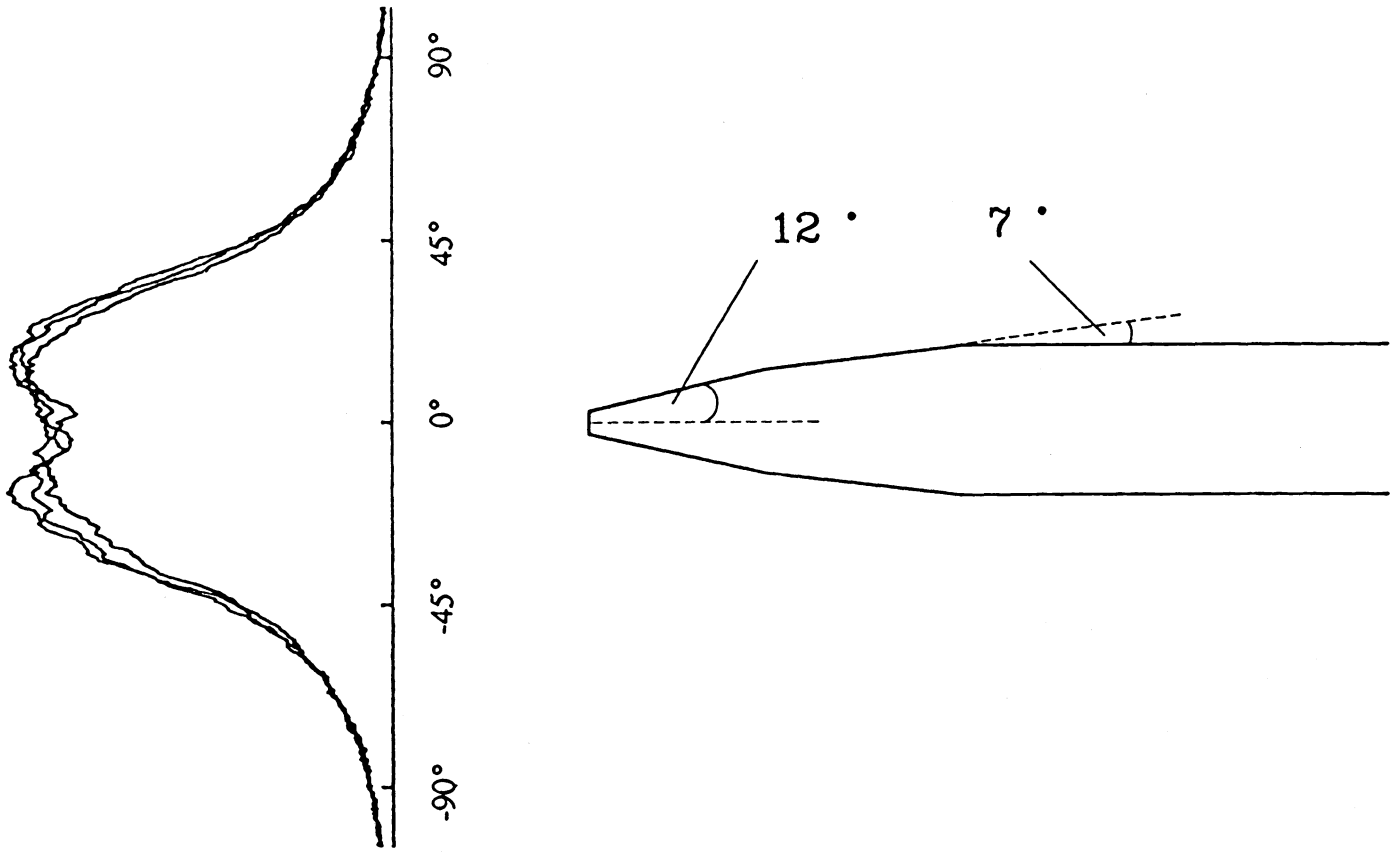

Fig. 2 Irradiation pattern of the biconic plastic fiber typ.

Preparation of the fiber end is maintained by a polishing device rotating the fiber in a special holder. Raytracing calculations have been performed to study the influence of different angles of the cones on the homogenity and aperture of the beam profile. The best results have been obtained with angles of 7° and 12°. Three different ray sections contribute to the beam profile. One is brought about by the forward part of axially unreflected rays leaving the fiber through the small plane end. This light is responsible for the flatness of the profile. The other contributions arise from internal reflections at both cone angles and subsequent refraction from the fiber. The aperture of the biconic plastic fiber is increased by a factor of nearly 2 as compared to the flat fiber tip. Since no additional optical elements are involved in the application system, transmittance is more than 80%. Due to the plastic core material, the fiber can only be used in combination with a liquid surrounding it for cooling, a condition met in the bladder filled with saline. Even at light powers of about 30 mW, the power density at the tip rise enough to cause melting processes in the air and subsequent destruction of the fiber tip.

2.3 Fiber optic endoadapter

An elegant method for endoscope assisted illumination of tissue during PDT is the transfer of red laserlight through the viewing channel of the instrument itself. With use of a fiberoptic endoadapter schematically shown in Fig. 3 light is coupled from a fiber into the endoscope via a dicroitic mirror.

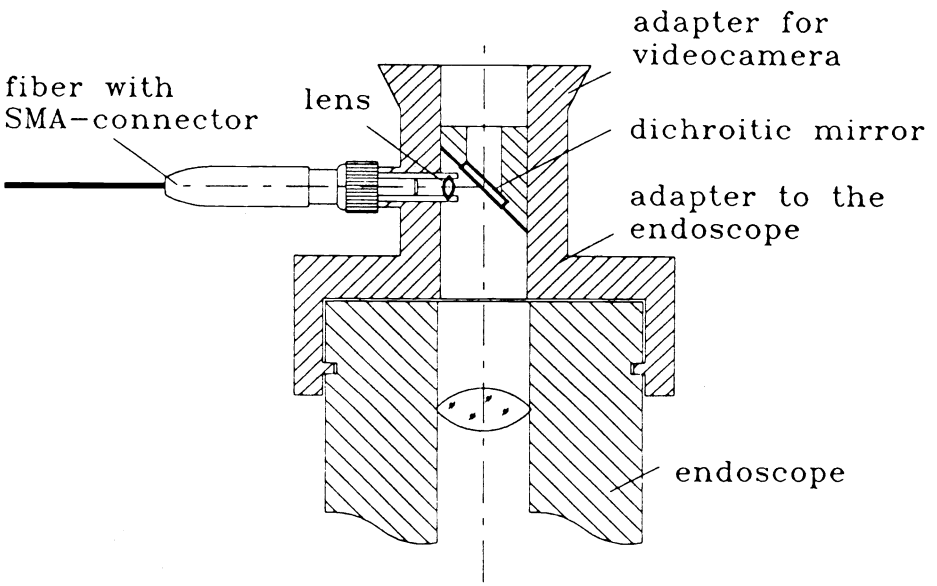

Fig. 3 Scheme of the fiberoptic endoadapter.

The plane end of the fiber is projected to the surface of the tissue by a convex lens including all the viewing components inserted in the endoscope. Homogeneous illumination of an area only slightly smaller than the aperture of the instrument itself is thus obtained. (Fig. 4)
A complete overlap may be achieved optimizing the components. Observation of the laser irradiated reddish area through the endoscope offers easy visual control of the illuminated area's position.
Adjustment of the dicroitic mirror allows for any fine correction necessary. In addition to the possibility of continous control during PDT, this method has the advantage of leaving the instrumentation channel free for conventional applications, such as for taking biopsies. Using specially marked thin catheters, the distance between the distal end of the endoscope and the tissue surface can be measured. This value together with the aperture of the endoscope can accurately determine the illuminated area. This forms the basis for calculation of the energy dose for PDT. The adapter can be coupled with rigid as well as with flexible endoscopes. To give an example, the adapter was used for treatment of small superficial lung cancer clearly localized at the bronchus wall by a rigid 90°-optics.

A series of light transmission tests shows the occurrence of light losses of about 50% in rigid instruments and more than 80% in flexible endoscopes. Despite this fact, low light-power densities of 100-200 mW/cm^2 are sufficient for PDT since the area to be illuminated is well below 1 cm^2. The temperature measured at the ocular optics of a flexible endoscope increases constantly when the power is coupled into the image bundle and reaches about 60° C at 2.5 W red laserlight.

Due to the autofluorescence of endoscope optics, this method cannot be used for diagnostic purposes. Violet light excites intense red fluorescence in the fiber optic bundles of flexible endoscopes as well as in the rod lenses of rigid instruments. When detected by an intensified CCD camera adapted to the endoscope, its contribution to the signal completely saturates the photocathode of the image intensifier.

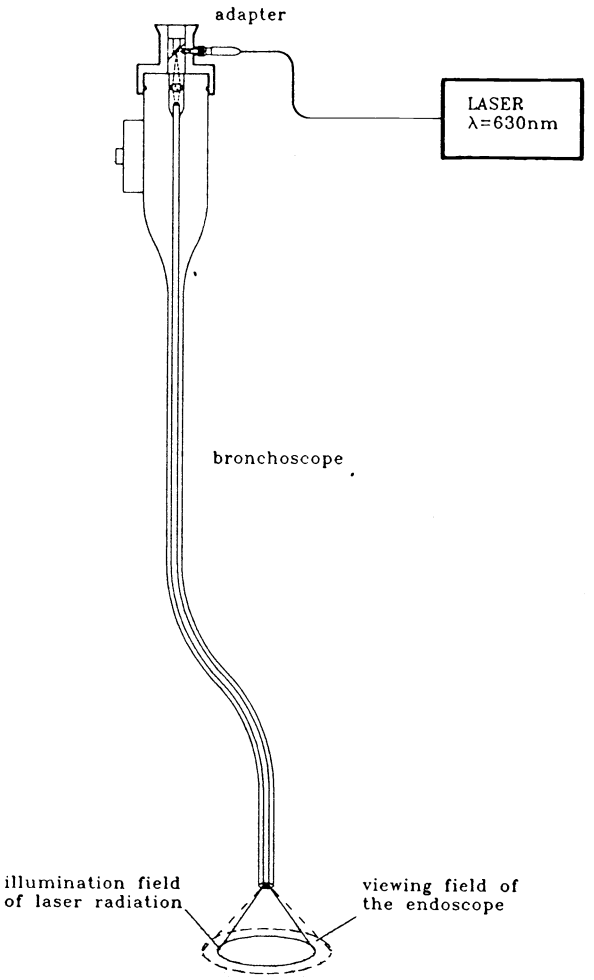

Fig. 4 Principle of operation of the endoadapter coupled to a flexible endoscope.

3. DISCUSSION

Fiber-coupled light application systems have been shown to be valuable in homogeneous irradiation of flat tissue surfaces, especially in combination with endoscopes. While the microlens probe can be used for photodynamic diagnostic and therapeutic purposes, the biconic fiber is used only for fluorescence excitation of photosensitized bladders filled with saline. Due to intense autofluorescence of the optics in endoscopes excited with violet light, the endoadapter is not suitable for photodynamic diagnosis, but this device was used successfully in photodynamic treatment of small tumor foci in the lung.

So far the three light application systems presented are lab versions. The quality of each probe, especially the biconic fibers, were tested by computer-assisted measurement of the beam profile. In most cases visual examination of an illuminated area is sufficient. Due to proven efficacy, microlens probes and endoadapter technology transfer have been initiated.

A new concept has been worked out concerning homogeneous irradiation of cylindrical, spherical and even irregular tissue geometries. On the basis of back-scattering layers, placed symmetrically around a central emitter, light homogeneity is improved considerably (4). In addition the application devices are designed to guarantee improved central positioning inside the hollow organs.

In conclusion, a breakthrough in the development of clinically acceptable light diffusers can be expected for all organs to be treated with PDD and PDT. Aided by devices which determine not only the light fluence rate in tissue but also the drug dose on site, photodynamic treatment modalities will confirm their position in clinical use.

4. ACKNOWLEDGEMENT

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