PORTABLE FLUORESCENCE MICROENDOSCOPE SYSTEM FOR SMARTPHONES

Pablo Aurelio Gómez García, Sebastião Pratavieira, Cristina Kurachi

Instituto de Física de São Carlos, São Carlos, Brasil

e-mail: pablo.aero.upm@gmail.com

Abstract: A portable microscope/microendoscope will be presented in this article. The system was specially designed for smartphones and taking into account its simplicity, will be able to bring this technology to almost every doctor's office. It is worth mentioning its flexibility of use, that allows several modes since all the components are interchangeable (the illumination LED, the lens, the dichroic mirror, etc) which permits different applications and also its economic price, that does not exceed US$ 300. The system can be used as a conventional microscope or as a microendoscope with a fiber bundle. Its first practical application will be to examine uterine tissue (in-vivo and ex-vivo) using proflavine as dye, but different applications are under evaluation.
Key-words: Microendoscopy, Fiber bundle, in-vivo microscopy, Diagnosis, Borescope, Image processing.

Introduction

Fluorescence microendoscopy systems have greatly evolved in the past few years, becoming a remarkable technology for its definitive implementation in hospitals all over the world [1,2]. Nowadays, there are three possible paths when a fluorescence microendoscopy system is going to be projected, with each one of them having great alternatives due to the relatively novelty of the technology (wide variety of systems can be found in the literature [3,4]. The first one would be to improve an existing design, either introducing a variation in the components setup, using new dyes, working with the system for new application, or improving the software for processing the images [3,5]. The second would be to design an entirely new system, given the great number of possibilities of this technology (new designs can be found every year in the literature [1,2,6]. In this case, the third alternative, which consist on simplify an existing setup in order to reach a simpler, cheaper and more comfortable system without losing performance, has been chosen [7,8,9].

A portable fluorescence microendoscope for smartphones that allows observing tissue at a cellular level resolution will be presented with its different applications.

Materials and methods

The system assembly - The high resolution portable microendoscope shown below (fig.1) will be described component by component on its basic configuration. In order to describe it in a organize manner it has been divided into the following subsystems:

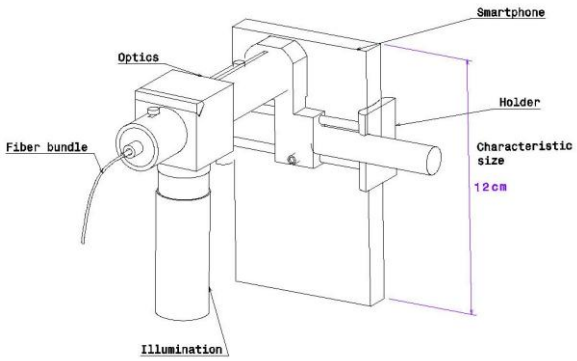

Figure 1: View of the complete system high resolution portable microendoscope assembly.

Optical:

1. Two identical lens (Edmund Optics 9mm Dia. x 12mm FL, MgF2 Coating, Achromatic Doublet Lens) that will act as an usual compound microscope [10,11] and can be moved using a screw through the grooves in order to change the magnifying power of it.
2. A dichroic mirror (485DCLP Dichroic (BS)) that will cut the electromagnetic radiation coming from the sample at 485nm so the camera only receives the corresponding to the fluorescence. The proflavine has excitation and emission peaks of 445nm and 515nm respectively, so this dichroic mirror will work, reflecting the light from the illumination (royal blue LED centered at 450nm) and letting pass the light from the sample fluorescence (at 515nm).
3. A pinhole placed between the lenses in order to correct optical aberrations coming from them and provide contrast to the image. The loss of resolution due to the pinhole exist, but it is not noticeable.

4. A fiber bundle composed by 10.000 single-mode fibers uniformly disposed linked to the system by a SMA connector. The bundle has a 4µm core to core distance and a total diameter of 720µm (these parameters will determine the resolution and the field of view of the system). [This piece can be replace with a support for a sample, so the system will turn onto a portable microscope]

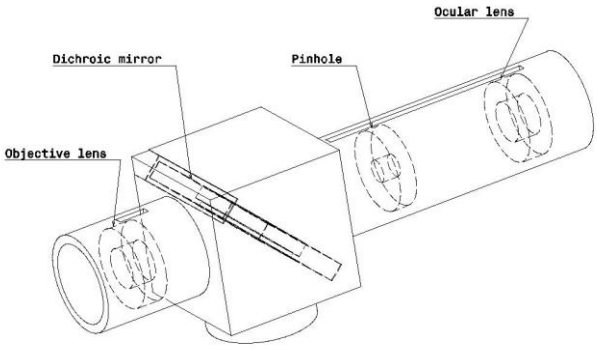

Figure 2: optical subsystem that works as a compound microscope with a dichroic mirror.

Illumination:

1. A royal-blue LED (Rebel Luxeon LXML-PR01-0500) which emission spectrum is between 440-460 nm and can work with a maximum continuous current of 700mA giving 910mW of power. This led can be change easily; by putting, for example, a white LED the system could became a conventional microscope.
2. A lens (Edmund Optics 12.5mm Dia. x 14mm FL, MgF2 Coating, Achromatic Doublet Lens) that together with the objective lens of the microscope, focus the illumination light into the sample or the fiber bundle.

Electronic:

1. Rechargeable Battery (TrustFire 18350 Li-ion 1200mAh 3.7V) that energizes the illumination.
2. Electronic circuit that receives the energy from the battery and supplies a continuous current to the LED. Also a button is installed in order to modify the amount of current and then the LED luminous power.

All these subsystem are supported by the main structure of the setup that is made of anodized black aluminum. It is worth stressing that almost all the components are easily interchangeable by others, turning the system useful for different applications.

Holder system:

1. Holder piece that attach the microendoscope to the smartphone. Due to its design it can serve for almost every device nowadays available in the market.
2. Conventional tripod that enables to place the system into a comfortable working position.

System operation - The resolution of the system (used as a microendoscope) is limited by the core-to-core distance of the fiber bundle, which is 4µm. The ideal resolution of the microscope is less than 1µm, but the practical it is near 4µm, so it is no worsening the total resolution of the system.

The contrast of a microscope is incompatible with a high resolution, so a optimum point needs to be elected in function of the studied sample. The contrast can be controlled with a diaphragm on the illumination system, which controls the percentage of the numerical aperture of the objective lens that is reached by the light cone coming from the sample. The fluorescence images with Proflavine are high contrasted, so it should not be a limitation.

The depth of field of a microscope is an important parameter since the motion precision of the objective lens depends on it. The depth of focus decreases when N.A (so resolution) and magnification of the microscopes increases. For this system this value could be estimated, at it first configuration about 15µm. The precision to focalize has been designed having into account this parameter.

The magnifying power can vary between 60X and 150X just adjusting the position of the two lenses. The microscopy image shape will be circular and it will fill the hole screen of an Iphone 5S (Apple Inc.) with the system operating on its maximum magnifying power.

The pinhole removes the beams coming from the out borders of the objective lens, correcting the aberration.

Table 1: Main characteristics of the system.

Property	Value
Resolution	~4µm
Magnifying power	60X-150X
Characteristic Size	120mm
Weight	0,25 kg
Main material	Aluminum
Tissue penetration	~50µm
Price	300 US$

A software to process images is being develop. It will calculate the size and the amount of cell nucleus and compare them with the total area of the image in order to create a relationship between these parameters and the state of the tissue. Also a study of the shape of these nucleus can be made, since the pixilation coming from the fiber bundle were partially avoided. The final objective is to bring this software to Android and IOS in order to process the images directly on the smartphone devices so having the entire operative diagnosis system just on every devices.

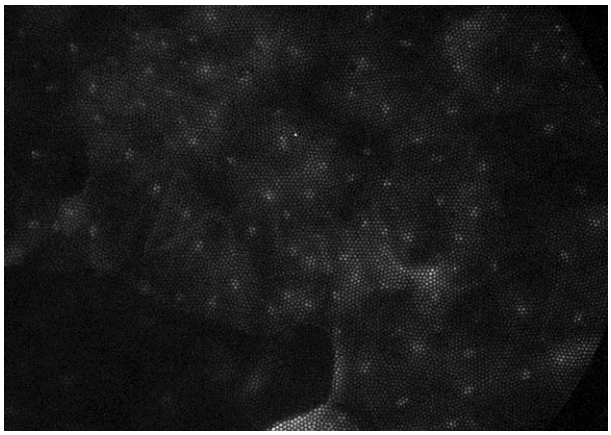

Figure 3: Typical image of a lip taking through the fiber bundle that shows the fluorescence of the Proflavine placed in the nucleus of the cells. Pixel size: 4µm, FOV: 720µm. [3].

The first dye will be Proflavine, that marks the nucleus of the cells, but by changing the excitation light and maybe the dichroic mirror, fluorescence from other fluorophores could be detected so having several diagnosis to contrast information.

The following table shows some of the fluorophores that could be detected with the system with their characteristic peaks of excitation and fluorescence emission. Each one of them indicates some properties or gives information about the state of the radiated tissue (for more information consult [12] and [13]).

Table 2: Excitation and emission peaks for several fluorophores.

Fluorophore	Excitation	Emission
Proflavine	455nm	515nm
NADH	340nm	450nm
Collagen	350nm	460nm
PPIX	405nm	630nm
FAD	450nm	530nm

Applications - The first practical application of the system will be to observe the in-vivo uterine tissue at a cellular level to discover possible damages caused by colon cancer. Also to observe ex-vivo uterine cells in order to make a instantly Papanicolau test. The system also can be use to observe other tissues since them were mucosa cells (in skin, for example, the illumination light at 450nm can't penetrate due to the superficial dead tissue).

Another possible application of the system could be examine non-accessible pieces of planes and engines. Nowadays the device used for that purpose is the borescope (rigid of flexible). The flexible borescope operation is similar to this portable microendoscope, it even use also a fiber bundle. The price of one of these devices with comparable characteristics is much higher than the system presented on this article.

The system will be greatly useful to observe any non-accessible element (tissue or mechanical pieces) so it could be applied to a wide range of medical diagnosis and mechanical pieces supervision. Taking into account its flexibility of configurations, several pieces of the system can be changed to adapt it for different applications.

Results

After testing the system operating with the fiber bundle, some images from lip, gingiva and the inferior part of the tongue have been taken. The nucleus of the cells can be successfully identified on them.

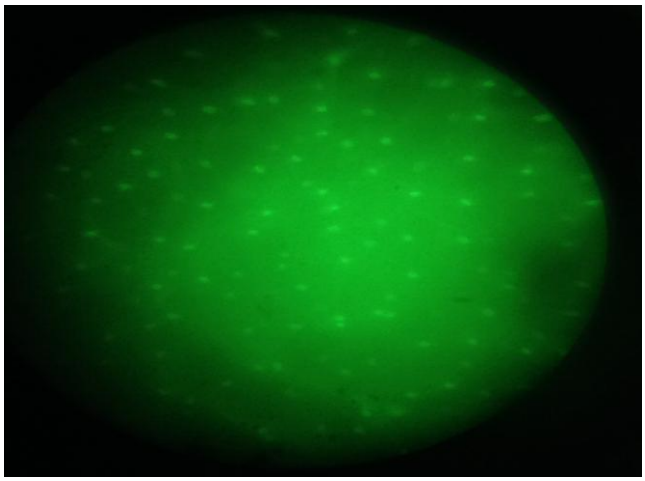

Figure 4: image of the gingiva taken with the system and a Smartphone. The image shows the nucleus of the cells with a resolution of 4µm and a FOV of 720µm.

Conclusion

A high resolution, simple, flexible, portable and cheap microendoscope system was develop for its use with any model of actual smartphone so every doctor that owns a smartphone could use it for a quick exam at a cellular level. This device along with the image software will be an entirely diagnosis system for several kinds of tissue and diseases. It also can be used in other areas like metal pieces supervision.

A cheaper model of the system could be achieve in order to make it accessible for every medical centers. In future designs possible deficiencies associates to the first prototype could be improve.

An arrange with a GRIN or ball lens at the distal end of the fiber bundle will led to higher resolutions since the illumination beam would be focalized onto a smaller area[3,4,5].

One of the common objectives of every microendoscopy systems is to observe deeper layers of tissue, in this direction, a version with optical elements at the distal end of the fiber bundle which could achieve

deeper penetration is being seek, since the scattering due to the tissue be avoided [4,5,14].

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