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Light-Emitting Woven Fabric for Treatment with Photodynamic Therapy and Monitoring of Actinic Keratosis

Yesim Oguz, Vladan Koncar, Cedric Cochrane and Serge Mordon

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Abstract

A successful photodynamic therapy (PDT) requires a specific photosensitizer, oxygen and light of a specific wavelength and power. Today photodynamic therapy (PDT) is administered to patients with light-emitting diode (LED) panels. These panels deliver a non-uniform light distribution on the human body parts, as the complex human anatomy is not a flat surface (head vertex, hand, shoulder, etc.). For an efficient photodynamic therapy (PDT), a light-emitting fabric (LEF) was woven from plastic optical fibers (POF) aiming at the treatment of dermatologic diseases such as actinic keratosis (AK). Plastic optical fibers (POF) (Toray, PGR-FB250) have been woven in textile in order to create macro-bendings, and thus emit out the injected light directly to the skin. The light intensity and light-emitting homogeneity of the LEF were improved thanks to Doehlert Experimental Design. During the treatment with PDT, the photosensitizers were activated in the cancerous cells. These cells may be visualized, as they show a characteristic fluorescence under UV light, which is called fluorescence diagnosis (FD). Therefore, it is proposed to modify the developed LEF for PDT to measure the fluorescence amount. For this aim, a part of POFs was cut out to observe the quantity of light that could be collected while the LEF was connected to a light source. The first prototypes showed the possibility of the illumination with the same LEF without losing the efficiency but also imaging the collected light.

Keywords: light emitting fabric (LEF), plastic optical fiber (POF), photodynamic therapy (PDT), weaving, fluorescence diagnosis (FD)

1. Introduction

The actinic keratosis (AK) is a pre-cancerous condition due to chronic UV light exposure that may develop into non-melanoma skin cancer [1, 2]. Thus, the treatment of AK is highly recommended. The AK lesions are characterized by red, scaly and crusty plaques or papules [3, 4]. This skin disease mainly affects fair-skinned individuals (face, bald head, forehead, etc.) [5].

There are many treatment options for AK. Cryosurgery, curettage and photodynamic therapy (PDT) are the common treatments. Cryosurgery is an operation to destroy the tissue by using freezing temperature performed with liquid nitrogen or carbon dioxide. This method is efficient on the thinner lesions but less successful on the thick lesions and may result in scarring [6]. Curettage is used to scrape of larger, hypertrophic lesions with a curette. The drawbacks of this technique are the necessity for a local anesthesia and the scars [7].

Photodynamic therapy (PDT) is a noninvasive method, particularly used to treat pre-cancerous or cancerous lesions with the combination of a photosensitizer and an appropriate light.

PDT has been increasingly used to treat AK, as it is efficient as other techniques given before but also has excellent cosmetic results, repeatable and does not kill the healthy cells (selective cell killing) [8, 9]. This treatment is also suitable for noncancerous lesions such as psoriatic, acne vulgaris, pre-cancerous lesions as AK and Bowen, and cancerous lesions as basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) [9, 10].

The PDT leads to selective destruction of the cancerous cells by activated photosensibilisant agent, methyl aminolevulinate (MAL) in Europe and 5-aminolevulinic acid (ALA) in USA. The photosensitizers (PS) are activated with an appropriate light, which is red light (630 nm) in Europe and blue light (450 nm) in USA in the presence of oxygen [11]. The activation of the PS generates singlet oxygen (1O_2) which causes chemical reactions inside the cancerous cells as they are rich with molecular oxygen [12] (**Figure 1**). This is so-called “selective cells killing.”

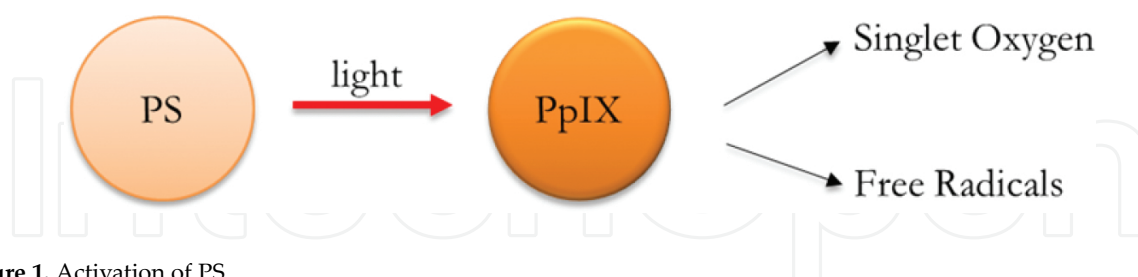


Figure 1. Activation of PS.

In Europe, PDT is performed by using a drug photosensitizer methyl aminolevulinate (MAL by Metvix, Galderma) on cancerous lesions and a 3-hour interval to start enlightenment [13]. The entire treated area is illuminated by a red light source (narrow spectrum around 630 nm) [14]. The activation of Metvix required a dose of 37 J/cm² [15, 16]. The light dose is determined by such factors as the size of the light field, the distance between the lamp and the surface of the skin, and the illumination duration. Therefore, it is not possible to treat numerous patients per day since the treatment of a single patient takes about 5 hours. It is possible to reduce the light exposition time by increasing the light dose, but the pain rate will also rise.

Today PDT is administered by light-emitting diode (LED) panels (**Figure 2**) [17]. This is an effective method without side effects with good cosmetic results. However, LEDs do not emit the same light dose over the entire treatment area and do not adapt to the irregularities of the body [13, 18]. Another disadvantage of this method is pain due to the dose of pure light that effective treatment with LED panels [19, 20]. Indeed, if the light output was less, we could limit the pain caused by the PDT.



Figure 2. LED panel light source (Aktelite CL 128, Galderma).

PDT needs to evolve despite its benefits, to make this treatment more effective and less painful. The market innovates and proposes inventions that allow surmounting the inconveniences of topical PDT with LED panels.

In order to maximize the comfort of the PDT and remove the disadvantages, Inserm (Institut National de la Santé et de la Recherche Médicale, France) and ENSAIT (École Nationale Supérieure des Arts et Industries Textiles, France) proposed replacing the LED panels by a LEF composed of PMMA optical fibers (POF) [21–23].

2. Development and optimization of a LEF

Optical fibers carry the light between the distal ends but do not emit light laterally in their natural state. There are three methods to bring out the light laterally. Mechanical process consists of creating scratches on the surface of the POF (sandblasting or toothed roll) [24]. Chemical process is by applying a solvent which degrades the outside of the fiber and passes light [25]. And finally the method of creating macro-bends (bindings in macroscopic size), to not satisfy the total internal reflection to create a leakage [26–29].

The optical fiber used in the experiments consists of a Poly MethylMethAcrylate (PMMA) core enveloped by a cladding made of fluorinated polymers. The core of the fiber has a refractive index greater than the cladding's, and therefore the light is confined thus completely reflected

(Snell's Law, Eq. 1). When a macro-bend is formed with an OF, light enters into the OF with an angle larger than the critical angle (Eq. 2). and it undergoes multiple reflections.

$$\sin \alpha n_{air} = \sin \theta_1 n_{core} \tag{1}$$

$$\theta_{critical} = \sin^{-1}(n_{cladding} / n_{core}) \tag{2}$$

As a consequence, when the fiber is bent, the light rays outside of the bend section will be emitted; the others will continue to meet internal reflection as seen in **Figure 3** [30–32].

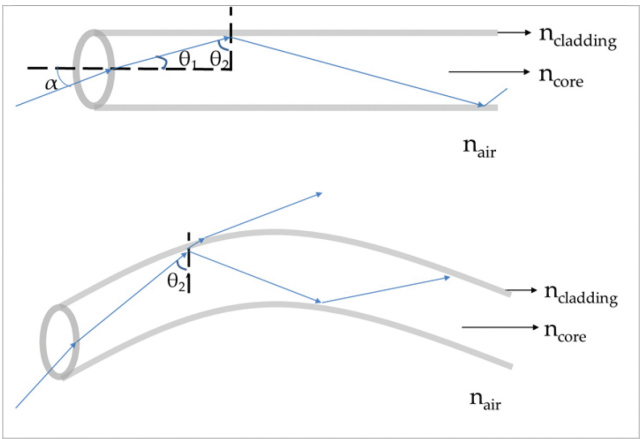


Figure 3. Multiple reflections in a bent optical fiber.

Weaving is a method of textile production which interlaces warp and weft yarns to form a fabric (**Figure 4**).

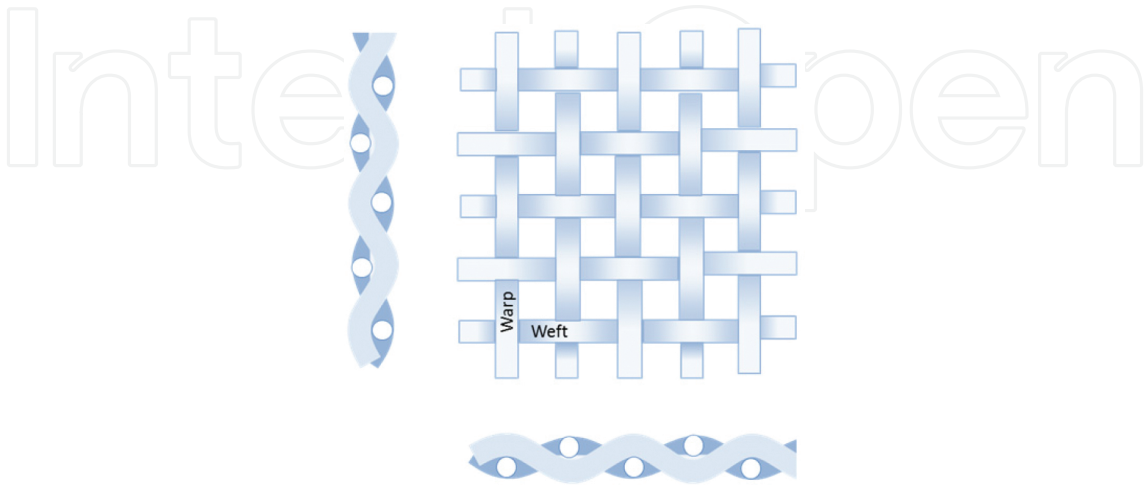


Figure 4. Scheme of a plain weave.

Thanks to the weaving technology, it is possible to create the macro-bends on the POFs as observed on the cross sections of the fabric in **Figure 5**.

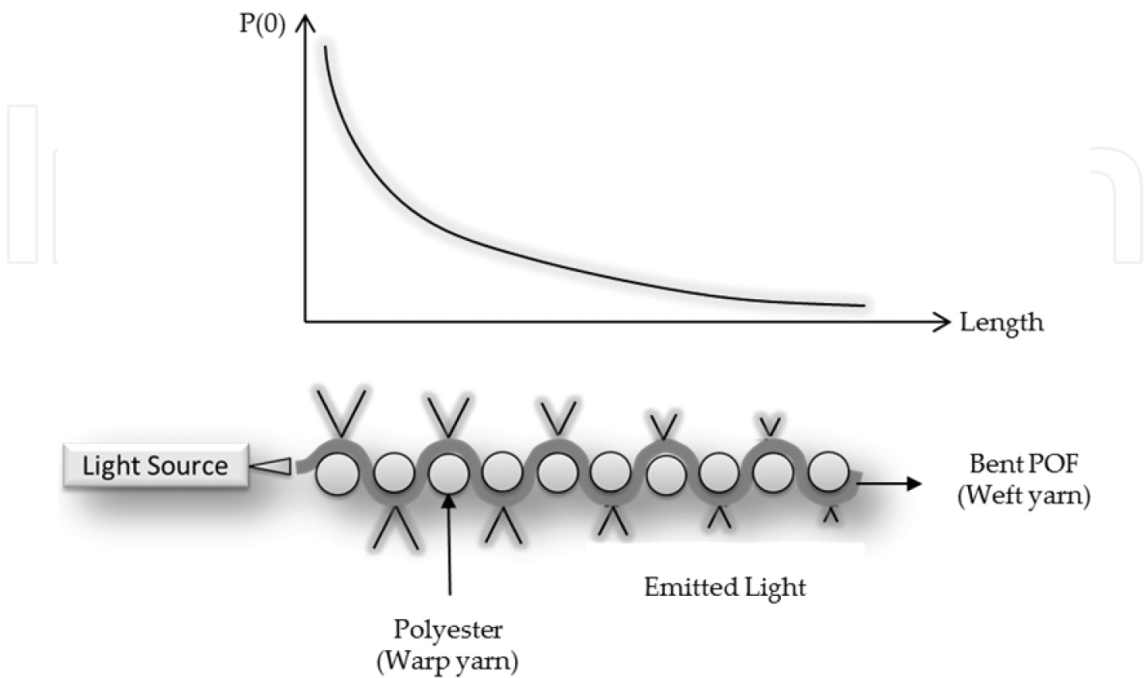


Figure 5. Bending loss in a POF inserted in a woven fabric.

It is possible to use different patterns to change the bending angles of the curvatures. There are three types of fundamental weaving patterns: plain weave, twill weave and satin weave (**Figure 6**) [33].

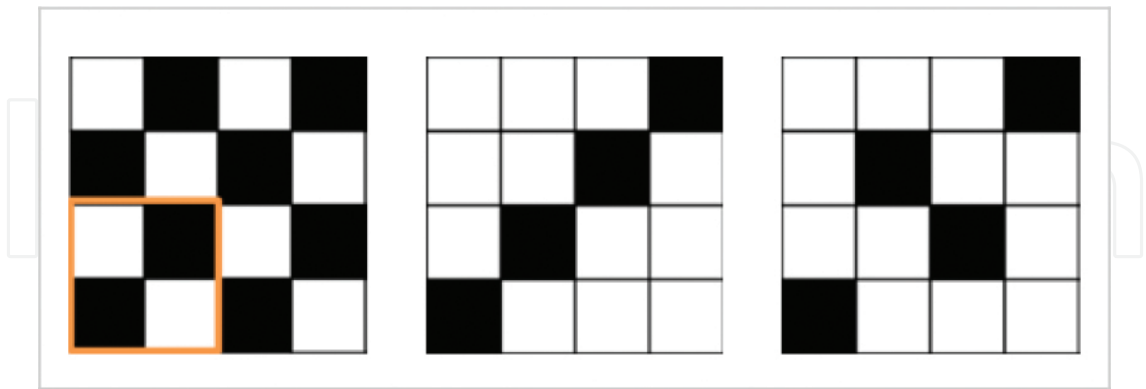


Figure 6. Fundamental Weaves: plain weave, twill 3-1, and satin 4, respectively.

Figure 6 shows the repeating pattern presentations of fundamental weaves. When the warp yarn is on the top of the weft yarn, it is presented in black; in the other case it is white. A weft float is designated as a number of warp yarns under the floating weft yarn between two intersections.

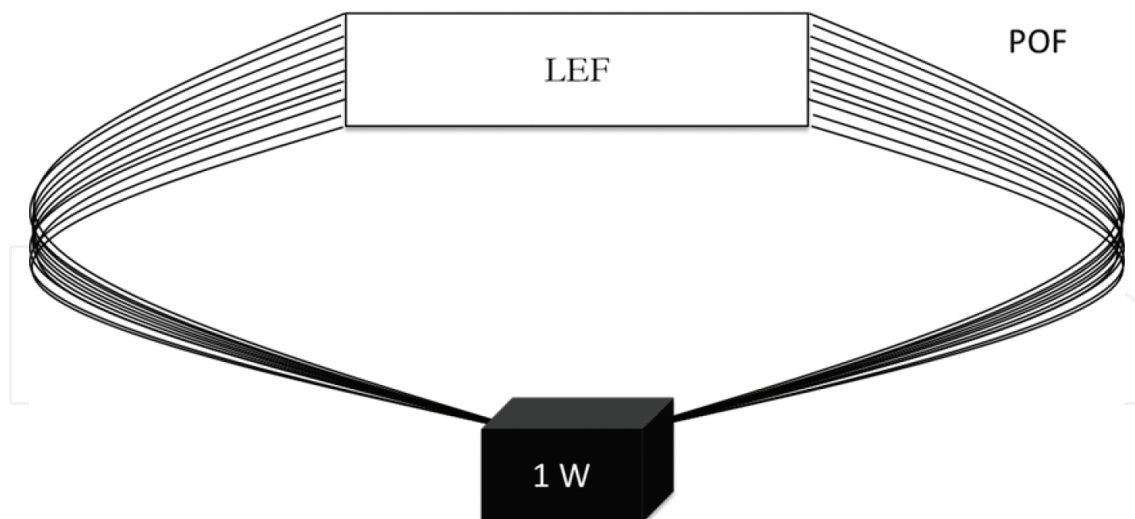


Figure 7. LEF connected to the light source.

The plain weave is the most basic of the three fundamental weaves. The weft thread passes successively above and below the warp yarn, and this order is reversed for each weft line (**Figures 4 and 6**).

The twill weave has a harness number equal to 1, and the crossing points form a diagonal (**Figure 6**). It consists of floats longer than plain weave.

The crossing points of the satin weave are defined with the harness number, and it is higher than 1 (**Figure 6**). Satin weave has longer floats compared to other fundamental weaves. This is the reason that we have used this weave to produce our fabrics. Longer floats prevent covering all the light-emitting POFs with warp yarns.

The quantity of the emitted light decreases with the distance to the light source as seen in **Figure 5**. The light transmission loss in an optical fiber is defined as the following equation according to the scientific literature [34, 35]:

$$\alpha = \frac{10}{L} \log \left[\frac{P(0)}{P(1)} \right] \quad (3)$$

where α represents the light transmission loss (dB/km), the length of the optical fiber (km), $P(0)$ represents optical input power, and $P(1)$ represents optical output power. Based on this formula (Eq. 3), different weaving patterns were woven to measure their attenuation in the same length.

The loss of the light in an OF depends on the radius of the bending curvature, the number of bending points and the wavelength of the signal.

For a successful treatment, a special pattern (patent WO 2012098488 A2) composed of three satin weaves was designed to obtain the same amount of bending, thus a homogenous light

distribution on the whole length of the fabric when it is connected to sources from both ends [36–38]. With this new pattern a homogenous light distribution was aimed for a successful PDT. Moreover, the LEF is connected to the light source from the both distal ends.

Polyester Sinterama (330 dTex)was used as warp yarn with a density of 20 per cm. Optical fiber PMMA Toray (250 μm) was used as a weft yarn with a yarn density of 37 per cm. The size of the luminous fabric is 21.5×5 cm. The total length of POF is about 60 cm but only 21.5 cm of POFs are woven in the middle. The both ends of the LEF were connected to the laser (1 W from both sides) as demonstrated in **Figure 7** and the light intensity (mW.cm^{-2}) was measured for each cm^2 of LEF length. For the medical application, it was important to obtain the light intensity values change within the limits of $\pm 20\%$, for a homogenous light distribution.

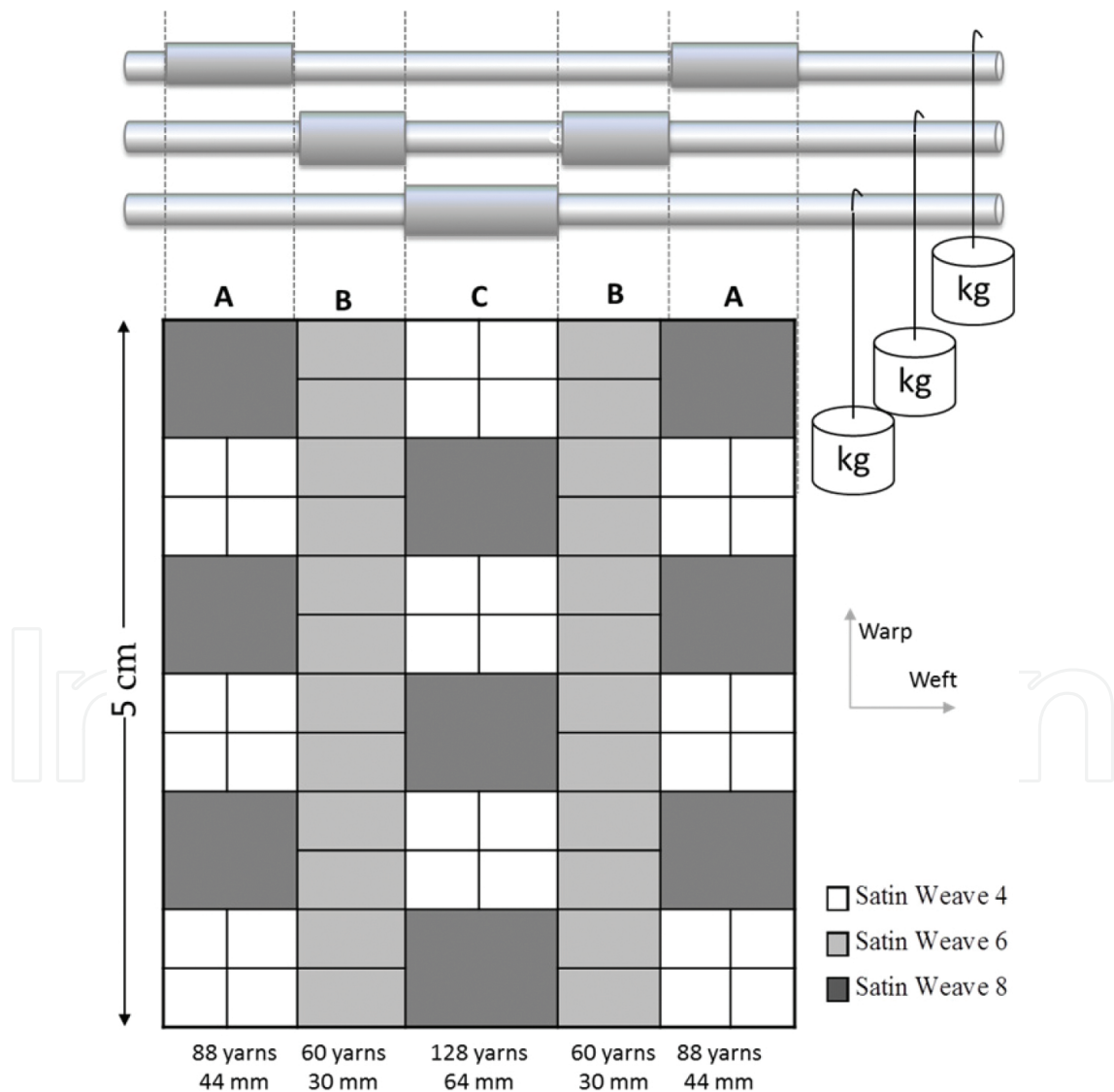


Figure 8. Scheme of the optimized weaving system.

An LEF which diffuses homogeneously light was obtained by using the designed pattern. However, it was also important to optimize the light intensity (mW.cm^{-2}) for a successful PDT. To improve the lateral light intensity and obtain an LEF that emits a consistent and powerful light at the same time, tension is added on the warp yarns during weaving [39]. Thanks to the added tension during weaving, it was possible to modify the curvatures of the optical fibers inserted into the LEF.

It is also very important to maintain the low light from the connectors on both sides to avoid feedback light toward the laser. This injection can increase the temperature of the laser sources, which can cause damage to the devices.

Three warp beams were prepared for three different weaving zones A, B, C and the loads were added on the beams, which were calculated with Doehlert experimental design. The samples are woven with the weaving machine (Dornier, HTVS8-SD). The optimized weaving system is shown diagrammatically below **Figure 8**.

In order to reduce the number of experiments, a three-factor Doehlert design was used in this work. This experimental design allows to find out the best parameters to optimize the results. The three weaving zones with different pattern combinations (A, B, C) were chosen as variables, and the three levels are chosen 40, 70 and 100 g/warp yarn, respectively. Fifteen samples were studied with the calculated tension parameters.

Furthermore, response surface methodology (RSM) graphics were generated with a Doehlert matrix design results. The graphics showed the emplacement of best results for the light intensity and light distribution homogeneity. Five more experiments were woven based on these parameters which should give the compromise result with a good light intensity and less heterogeneity ($12.8 \pm 3 \text{ mW.cm}^{-2}.\text{W}^{-1}$). The sample number 15 gave the best result as predicted and proved the reality of this approach (**Figure 9**). This was the optimal sample with given pattern, warp/weft material and density.

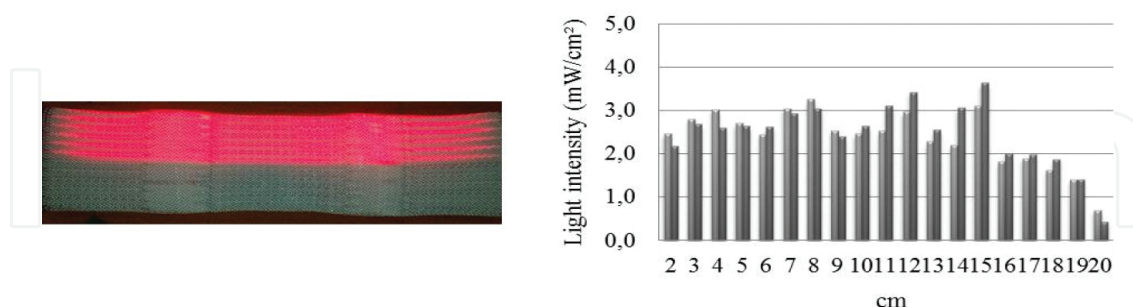


Figure 9. Light distribution of the optimized with Doehlert Experimental Design.

This diffuser light textile meets the basic requirements for PDT: uniform distribution of light and flexibility. The great light diffusers (500 cm^2) textiles can be easily manufactured and can be used not only on the skin but also in the peritoneal or pleural cavities.

PDT administrated with LEF will improve the effectiveness of treatment and make the procedure almost painless. Clinical trials were started (at CHR and Klinikum Vest) on 55

patients. For each patient, half of lesions were treated with conventional therapy, and the other half with the smart textiles, to compare the pain and the effectiveness on the same patient. The results are expected before 2017. Whenever the convincing results are provided, this method will replace the current treatments with the LED panels.

In addition, the new procedure will allow to treating multiple patients simultaneously, with less pain, under the supervision of doctors. Thanks to miniature laser sources and their decreasing prices, this procedure may also be transformed into a portable medical device that will allow patients to be active (**Figure 10**).



Figure 10. The PDT with woven LEF by ENSAIT (a), LEF inserted helmet design (b).

As the phototherapy has a good future, there are many concurrences developed to improve the procedure existent. Philips has developed a new technology called “BlueControl” which is a portable light therapy device for the treatment of Psoriasis Vulgaris. This device provides a treatment of 30 minutes per lesion, through the benefits of blue LED light without UV (453 nm) [40, 41].

Philips also developed the “Bilirubin blanket,” made of woven fabric consisting of stitched tiny blue LED lights. This device is used for the treatment of jaundice which is a condition caused by high levels of bilirubin in the blood.

And Metvix Galderma has proposed PDT daylight as an alternative to the PDT conventional. The daylight PDT allows patients to be active and under the sun during treatment, contrary to illumination with a fixed wavelength in clinical place [42, 43]. Daylight PDT has a good efficiency and is less painful thanks to low light output compared to the conventional method. However, this new method has several disadvantages. Allowing the patient to prepare the area to be treated may cause a lack of control of the light dose and time of exposure. In addition, the patient is dependent on the season and weather conditions.

In conclusion, PDT with flexible woven LEF by ENSAIT overcomes the obstacles of the other alternatives. One of the most important advantages of this technology is the possibility of using different wavelengths and dose of light by just changing the light source, thus allowing the treatment of different diseases (red for AK, blue for Jaundice, etc.). Also the possibility of using miniature lasers prevents the lack of control of the light dose or time exposure. That makes the treatment applicable any time or anywhere without depending on the weather conditions.

3. Future prospects of monitoring the cancerous cells with an LEF

During the PDT, the accumulated MAL is converted into active Protoporphyrine IX (PpIX) with the light exposure in cancerous cells. These PpIX are characterized by a red fluorescent color when viewed with a Wood lamp which uses ultraviolet (UV) light to examine the skin ([13, 44–47]; **Figure 11**). It is therefore possible to monitor the amount of PpIX in tissues by measuring the fluorescence before or during treatment. This procedure is called fluorescence diagnosis (FD) [13, 45, 48].

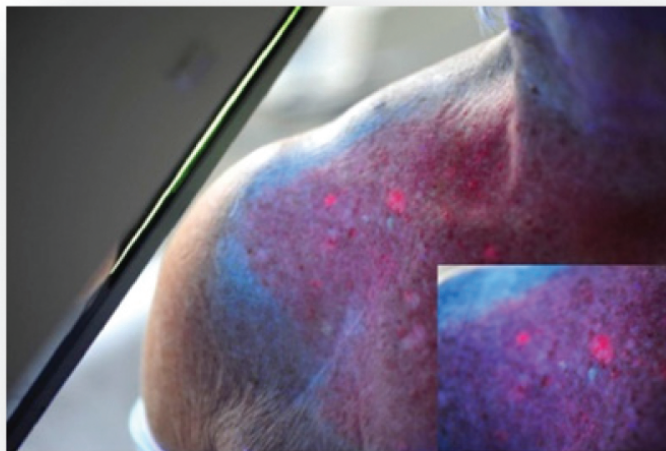


Figure 11. Imaging of PpIX after illumination with Wood Lamp to monitor the cancerous cells.

The use of LEF already developed in our research as a tool for FD is also investigated in this work. The aim was to use the same LEF for not only treating but also monitoring the cancerous cells. For this purpose, first of all, 1 fiber out of every 20 fiber is cut out from the connector on both edges as in **Figure 12**, and 1 W light is injected inside the both connectors. Secondly, the collected light from the fibers cut out (shown with second power meter sensor in **Figure 12**, and the light puissance of LEF were measured (shown with first power meter sensor in **Figure 12**).

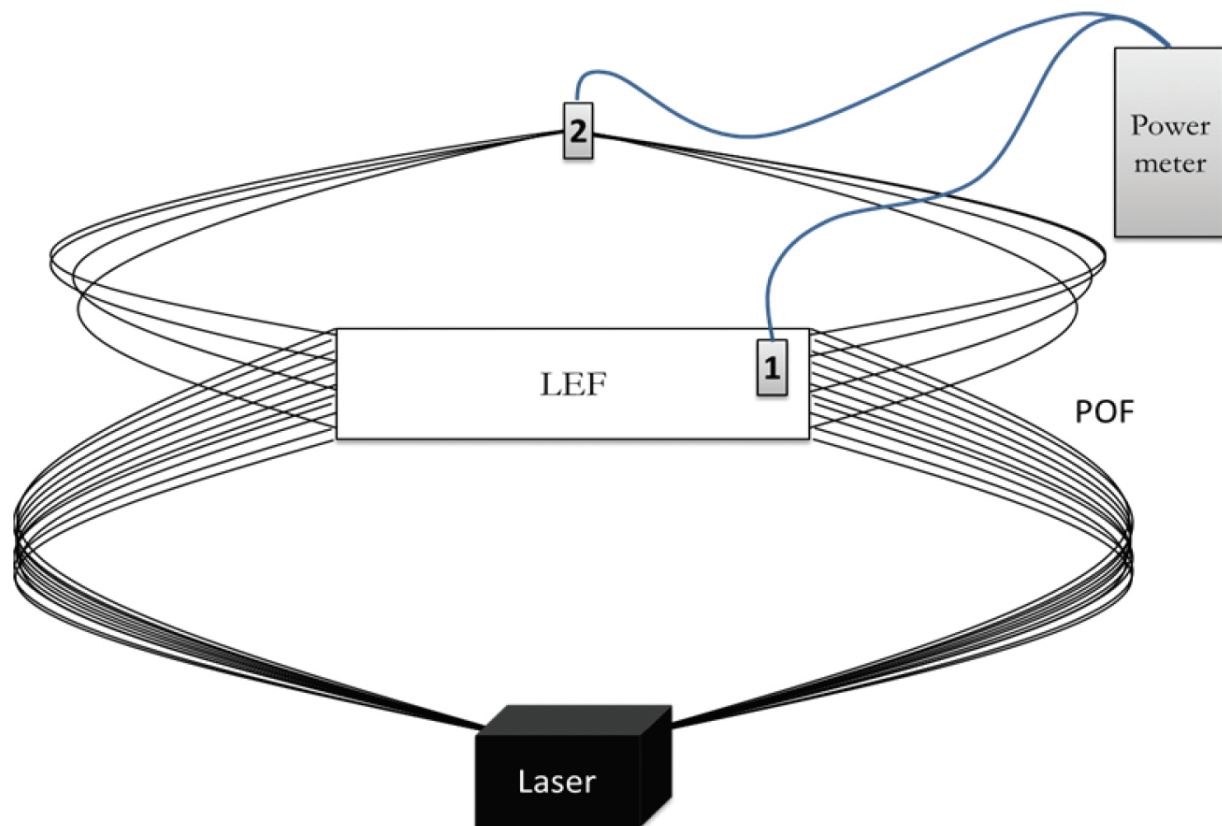


Figure 12. Measure method for monitoring application.

Furthermore, with the aim of finding the best ratio between the number of POF for the treatment and for the monitoring, the measures were repeated on the same LEF by cutting out 1 of 10 POF, 1 of 5 POF and 1 of 2 POF for using as a monitor. The results are given below for each experience.

As given in **Figure 13**, the collected information from the POFs cut out for the monitoring was increased with the number of the monitoring POFs. In the same time, there was no significant decrease of light power on the LEF, except for the last trial with one of two POFs. This could be explained by the light transmission of the neighbor POFs. On this wise, the emitted light from the neighbor POFs may penetrate inside the concerning fiber and keep stable the light intensity of the LEF in a 1 cm² area.

However, the monitoring sample with one of two POFs showed low light output from the LEF surface and the monitoring fibers. It shows that the monitoring POFs which are not covered with several bended fibers may not accumulate enough quantity of scattered light from the neighbor POFs.

The results were obtained from an LEF woven with 37 POFs/cm. The best compromise was using one of five POFs as monitoring fibers which showed a good light output from the monitoring fibers without losing the lateral light emission power.

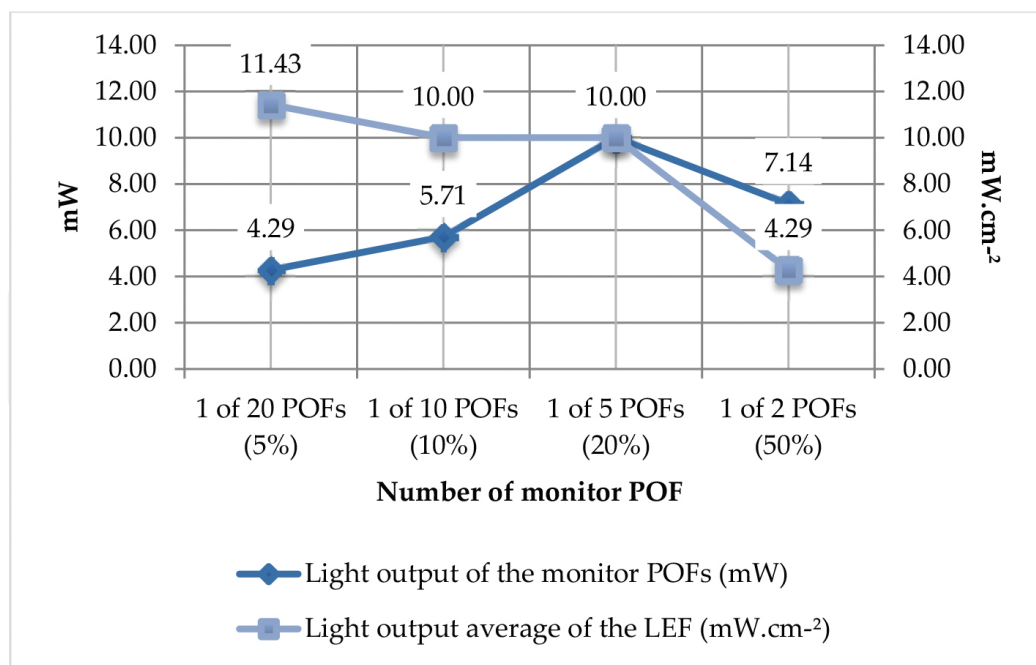


Figure 13. Monitoring measure results.

4. Conclusion

An LEF has been developed and optimized to use in PDT, thanks to the weaving technology and Doehlert experimental design. Furthermore, it is proposed to use the LEF to observe the cancerous cells that are visualized as red fluorescent after illuminated with UV light. The procedure requires a treatment with red light for a specific time period, and then diffuses a UV light to measure the fluorescence quantity to observe if there are more cancerous cells. The trials to prove the possibility of using a part of POFs as a monitoring tool were experienced successfully and worked well.

This work has demonstrated the possibility of treating and then controlling the amount of remaining tumor cells with the same LEF. There are similar examples in dentistry, such as fluorescence signal detection with polymeric optical fiber. The next step will be a simulation of the fluorescence diagnosis by injecting fluorescence light to the surface of LEF and measuring the output from the monitor optical fibers.

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