Results in Physics 11 (2018) 975–983

Contents lists available at ScienceDirect

Results in Physics

journal homepage: www.elsevier.com/locate/rinp

Light source optimizing in a biphotonic vein finder device: Experimental and theoretical analysis

A. Madrid García*, P. R. Horche

Departamento de Tecnología Fotónica y Bioingeniería, Universidad Politécnica de Madrid, Madrid, Spain

ARTICLE INFO

Keywords:
Vein finder
Biophotonics
LED
Biomedical device
Skin optics
Cannulation
Intravenous therapy
Blood extraction
Transillumination
3D printing
MATLAB

ABSTRACT

Solutions oriented to non-invasive superficial veins visualization by physicians are not numerous neither cheap. In spite of the advantages these solutions can provide in cannulation or venepuncture processes, especially in some population groups, their use is not widespread. Making use of an own designed 3D printed model, we experimentally studied the feasibility of using Ultra-Bright light-emitting diodes (LEDs) of different optical features to facilitate the visualization of the veins in a transillumination biophotonic approach.

Introduction

According to some studies, around eighty per cent of the hospitalized patients receive a peripheral intravenous (I.V) cannulation [1]. In fact, although it is considered as a routine procedure, their related complications are often unknown and undervalued. Some associated medical complications, (which also have attached other complications such as economical indemnities) derived from unsuccessful cannulation procedures, can be bacterial infection, extravasation, phlebitis, thrombosis, embolism or nerve damage [2].

A published study in the *British Journal of Anaesthesia* showed the ratio of difficult venepuncture cases in different populations group. The percentage of those is shown in Fig. 1.

The amount of adipose tissue surrounding vessels, the loss of muscle tone, a high melanin concentration, a blood flow reduction or an injured skin are some cases which can prevent a successful venepuncture process at the first attempt.

Furthermore, there are some cases in which choosing the most suitable vein is even more important than doing the cannulation or venepuncture process accurately: avoiding sensitive places derived from venous fibrosis, local infections or inflammations, fistulae or vascular grafts, and patients with haemophilia [4] are some examples of that situations. Aside from venepuncture, a vein visualization system could also abe useful in some other medical procedures, like pollicization [5] or sclerotherapy [6].

For the reasons given above, we study different optical configurations in a biophotonic device, to maximize veins visualization and to assess the potential benefits of using these devices in the healthcare assessment.

State of the art

Nowadays, there are different approaches by which a physician can see in a non-invasive way the patient's vessel. A summary of all of them is presented in Fig. 2.

1. Ultrasound (US) biomedical imaging systems have been used for assisting cannulation from a long time ago. The non-invasive technique, the real-time acquisition and the portable features have done from US one of the most common ways for I.V. procedure. Site-Rite Prevue® Ultrasound System, is an example of US systems already used.
2. Inside biophotonic based solutions there are two main alternatives:
   2.1. Solutions that take advantage of *Near Infrared (NIR) spectroscopy principles*: these solutions project over the skin surface a map of the blood vasculature employing a visible wavelength. The projections are achieved by previously radiating the skin surface with NIR light and quantifying the amount of light

* Corresponding author.
E-mail addresses: alfredo.madrid.garcia@alumnos.upm.es (A. Madrid García), p.rhorche@upm.es (P. R. Horche).

https://doi.org/10.1016/j.rinp.2018.10.033
Received 11 August 2018; Received in revised form 23 October 2018; Accepted 23 October 2018
Available online 03 November 2018

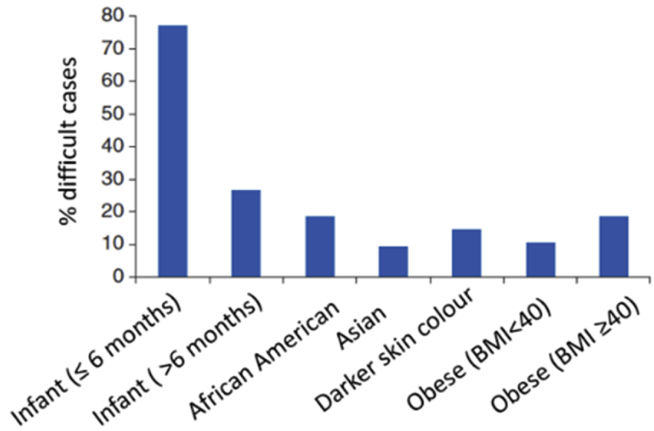

Fig. 1. Percentage of cannulation difficult cases [3].

absorbed by the blood (haemoglobin) and reflected by surrounding tissues. The device will capture the information, process the data and finally project over the skin surface the venous distribution. AccuVein®, VeinViewer® and IV-eye®, are the most well-known devices which take advantage of this principle.

2.2. Solutions that take advantage of visible light together with skin optics properties, also known as *transillumination* solutions: they are based on the use of *LED technology*. Skin surface is irradiated with a light source of an appropriate visible wavelength, allowing directly the visualization of the veins by differences in the biological and physical tissues properties. Absorption, scattering and reflexion of the light inside skin tissue will determine the visualization since not all wavelengths are able to penetrate enough into the skin. Therefore, the emitting wavelength in this approach is consciously chosen to maximize the light penetration. Absorption differences between skin chromophores and blood chromophores will allow veins visualization. Venoscope®, Veinlite®, Wee-Sight Transilluminator® and Illumivein® solutions follow this approach. The intensity of the light reflected is usually higher than the light transmitted to the vessels. Therefore, difficulties of superficial vein visualization arise, given that too powerful light and shadows patterns could emerge. To overcome this issue, *side-transillumination method* can be used instead of transillumination, which uniformly illuminates a small region of the skin to reduce the shadows and allowing light penetration up to 6 mm in depth.

3. Smartphones have also been used in the vein visualization task by acquiring reflectance information thanks to an RGB conventional camera and multispectral Wiener estimation [7].
4. Finally, other approaches not fully developed, are being under research such as a penetration method using NIR [8], robotic systems or pressure sensors to facilitate blood extraction [9].

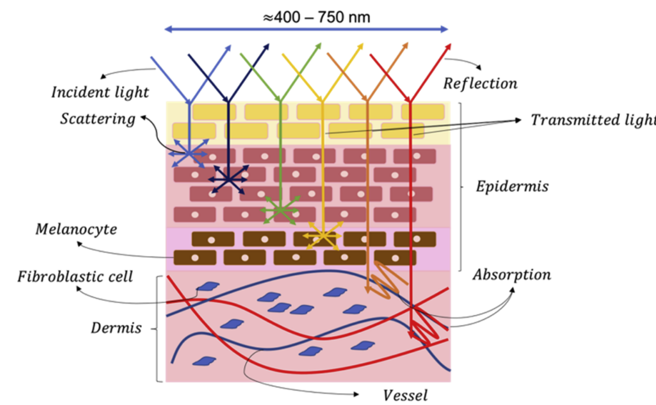

Fig. 3. Light propagation in the skin schema.

A fully description and comparison among the approaches presented in Fig. 2, can be found in [10]. Although, ultrasound systems have been demonstrated to be useful [11], they are not as affordable as other solutions based on biophotonics which also facilitate the cannulation procedure [12,13]. Performance differences between NIR and transillumination solutions have also been discussed in recent years [14,15].

Nowadays, transillumination methods are becoming more popular since they present two major benefits over those based on NIR principles: portability and cost. However, available transillumination commercial solutions differ significantly among them. The number of light sources employed, from two light-emitting diodes up to thirty-two, the wavelength, or the luminous intensity are some of the optical parameters which can vary from one commercial solution to another.

In this study, we identified and analysed the light source parameters that can affect the veins visualization, since there is not an agreement of the optimal light source features to be employed in these biomedical devices. Results derived from this study can be useful to develop an accurate vein seeker device or to understand and choose wisely from current transillumination solutions.

Light transport in the skin

Skin tissue structure is designed to reduce light penetration through a successive layer structure with different composition and properties

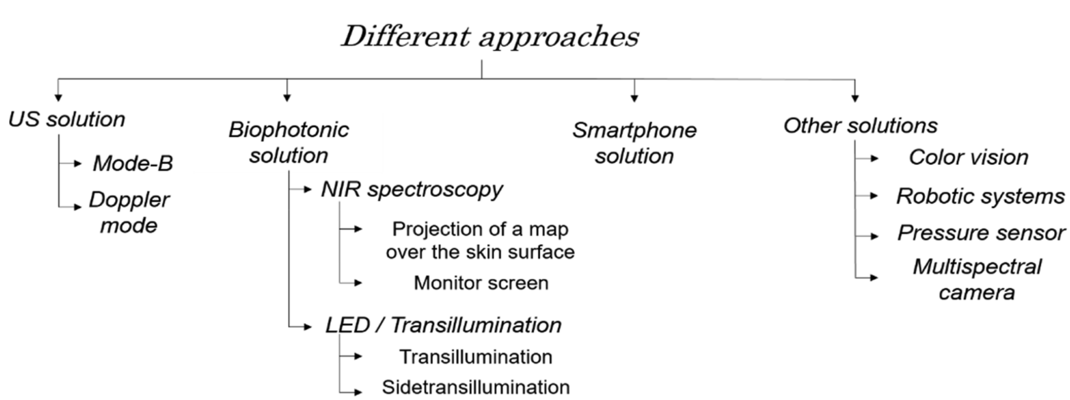

Fig. 2. Different non-invasive vein visualization approaches.

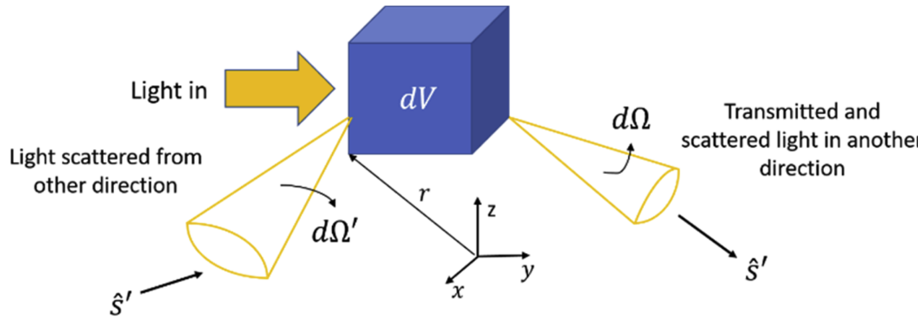

Fig. 4. Light propagation schema in RTT theory.

Table 1
Design parameters.

Critical Parameters
Wavelength (λ): distance between consecutive crests on a periodic wave of the light emitted by the LED diode. Only wavelengths inside the visible range, 380–750 nm, will be considered
Luminosity (I_V): luminous power per unit solid angle emitted by the LED diode in a particular direction. The studied luminosity range in this study varies from 150 mcd to 15.000 mcd
Angle (α): angle at which the light emitted by the LED diode is distributed. Angles between 15° and 140° were studied
Other Parameters
Number of light sources (**N**): number of LEDs used in each device. Two different values were considered: 11 and 20
Polychromatic light (**PL**): devices with more than one different LED and wavelength will be considered as polychromatic light devices
Size of the light source (**S**): size of the LED diode lens. Two possible values were considered: 3 mm and 5 mm

[16,17]. Differences in these optical, physical and biological properties explain why vessels can be seen when the skin is irradiated with visible light of an appropriate wavelength. Inside optical and physical phenomena, reflection, scattering and absorption plays a key role. Whereas the first one, reflection, limit the light propagation at the first light-skin encounter, absorption restricts light penetration and scattering deviates the light trajectory inside the skin [18]. Therefore, it is estimated that about the 4%–7% of the light is reflected as a consequence of refractive index differences between air and skin. Considering that the longer the wavelength of the light, the deeper the penetration [19], as it is represented in Fig. 3, the transmitted visible light will not penetrate deeper than 4–5 mm inside the skin.

In human tissues, scattering is the dominant factor affecting light propagation. Inside skin, keratin and melanin from the epidermis form the main scattering barrier. In dermis layer, where blood vessels are located, scattering is produced by heterogeneities derived from the variable cellular components presented in the different sublayers (e.g. stratum corneum or basale) and by different molecular concentrations. Due to the great number of scatterers presented in the media -obstacles that deviate the light path from a straight trajectory-, mathematical models like the *Radiation Transport Theory* (RTT) have been developed to describe light propagation when multiple scattering phenomena are presented. This theory is based on tracking photon changes (energy flow) in an infinitesimal volume dV, within differential solid angle $d\Omega$ around $\hat{s}$ direction, Fig. 4. Changes in energy flow can be caused by incoming, outgoing, absorbed and emitted photons, that have been scattered from one scatterer (e.g. elastin or collagen fibres) to the light from other scatterers existing in the media. Energy flow implies energy conservation, so, RTT can be interpreted as an energy conservation problem. A further description of this theory can be found in [20].

The study of RTT in human skin is done by using the *Diffusion Approximation* which assumes that light is able to penetrate deeper into the tissue, since absorption is lower than scattering [21,22].

However, physical responses derived from a tissue after having been irradiated with an incident light beam not only depends on the tissue biological properties but also on the features of the light source. Factors such as the wavelength of the incident light, the optical power emitted by the light source, the exposure rate (W/cm^2), the irradiated area, the irradiation time, the number of pulses and their duration and the polarization state will influence that tissue response. The exposure size of the light also affects the effective penetration depth, achieving a deeper penetration when the intensity given by the source of light is greater. L. Fodor et al. carried out a description of some of these factors in [23].

Therefore, in medical applications or devices which take advantage of the interactions between light and matter (i.e. biophotonic applications), like the vein finder, the properties of the light source should not be considered in an isolate way, but also tissue properties and physical optical phenomena should be taken into consideration at the same time.

Experimental set up

Design parameters

To determine the most suitable light-source and structural features in a biophotonic vein finder approach device that optimize the visualization, we considered and ranked different parameters that could affect vein visualization in a biophotonic approach, Table 1. From top to bottom, and according to our experiments, we established the most decisive physical parameters that could be involved in the visualization. Critical parameters are those parameters that must be satisfied to visualize vessels, otherwise visualization will not be achieved. Other parameters are those than can modify the visualization but are not mandatory to visualize vessels.

Implemented devices

Different devices were built to compare they visualization performance depending on the different parameters' settings. Table 2 summarizes the different devices as well as their features. To identify them, we built their name according the next schema:

W(avelength) (nm)	X (Colour name's initial: Orange, Red, Combined)	**N** (umber of LEDs)	YY	**S** (ize of LEDs) (mm)	Y

Case design of WON11S5, WRN11S5, WCN11S5 devices were retrieved from [24]. In addition, by using a 3D printing approach, with polylactic acid as the chosen structural material, the rest of the devices were built.

Ergonomic and mobile features were considered; therefore, a minimalist, small and portable device was designed. Energy supply is provided by an accumulator and light sources are distributed along the ring to achieve a uniform and homogeneous illumination inside the FOV (27 mm). Both structural and electrical schemas are shown in Fig. 5.

Table 2
Datasheet of the devices.

Visual design	Name	λ (nm)	I_V (mcd)	α°	N	PL	S (mm)
	WON11S5	600–610	4.200–5.800	15	11	N	5
	WRN11S5	620–630	4.900–6.300	35	11	N	5
	WCN11S5	600–610	4.200–5.800	15	5	Y	5
		620–630	4.900–6.300	35	6		6
	WON20S3	600–610	7.000–8.000	30	20	N	3
	WRN20S3	650–670	5.800–7.000	30	20	N	3
	WCN20S3	600–610	7.000–8.000	30	10	Y	3
		650–670	5.800–7.000	30	10		3
	WGN20S3	520–530	8.400–10.000	30	20	N	3

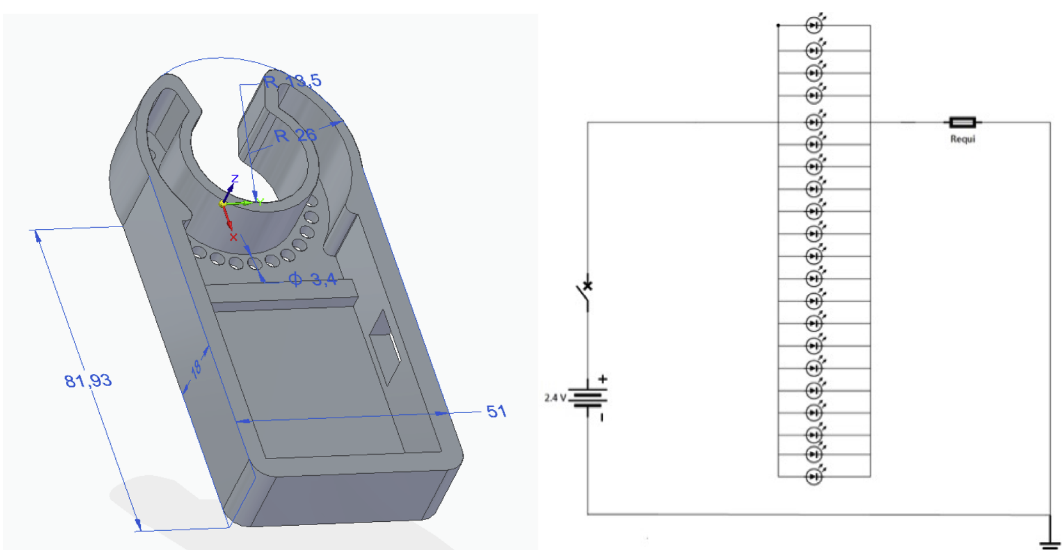

Fig. 5. Design process of the devices.

Chosen light sources decision was based on the theoretical penetration power of the different wavelengths, as was seen in Fig. 3, and also on a light source experimental comparison. In Fig. 6, all the different tested and evaluated light sources can be found:

Wavelength

Veins visualization can only be achieved by irradiating the skin with a light of an appropriate wavelength, otherwise light would not penetrate enough into the skin to reach blood vessels and to be reflected again to the surface. Therefore, the most decisive factor of a veins visualization system, in a transillumination approach, is the wavelength of the light employed. An evaluation of the different light sources with different wavelengths was carried out in order to assess skin absorption and veins visualization. We tested light sources with a wavelength range from 465 to 640 nm. Only light sources above a wavelength threshold that we set in 580 nm (Fig. 6. 3b), deep enough in the skin

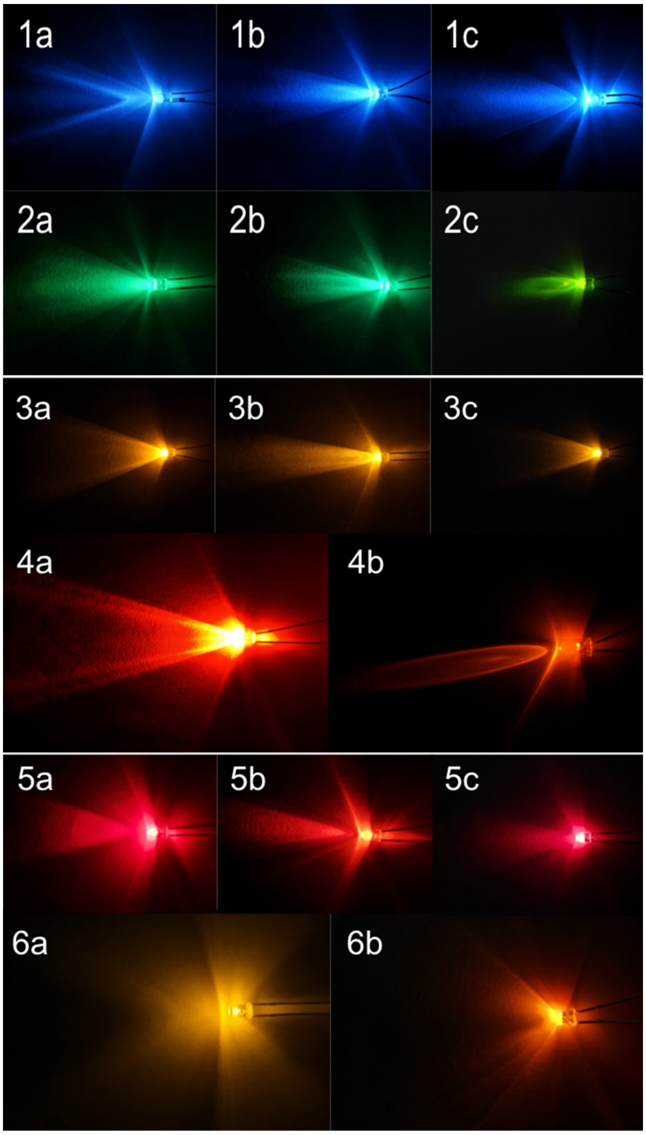

Fig. 6. Light source study. 1a) I_V:12.000–15.000 mcd, α:30°, λ: 465–475 nm. 1b) I_V: 1.600–4.200 mcd, α:15°, λ: 465–475 nm. 1c) I_V: 330–500 mcd, α:30°, λ: 465–475 nm. 2a) I_V: 8.400–10.000 mcd, α:30°, λ: 520–530 nm. 2b) I_V: 7.000–15.000, α:15°, λ: 518–524 nm. 2c) I_V: 150–330 mcd, α: 30°, λ: 570 nm. 3a) I_V: 5.800–7.000 mcd, α: 30°, λ: 585–595 nm. 3b) I_V: 5.500–9.000 mcd, α:15°, λ: 588–594 nm. 3c) I_V: 120–150 mcd, α: 30°, λ: 585–595 nm. 4a) I_V: 7.000–8.000 mcd, α:30°, λ: 600–610 nm. 4b) I_V: 4.200–5.800 mcd, α: 15°, λ: 600–610 nm. 5a) I_V: 5.800–7.000 mcd, α:30°, λ: 650–670 nm. 5b) I_V: 2.200–4.200 mcd, α: 15°, λ: 620–625 nm. 5c) I_V: 500–700 mcd, α:30°, λ: 640 nm. 6a) I_V: 330–500 mcd, α:120°, λ: 585–595 nm. 6b) I_V: 220–330 mcd, α:140°, λ: 600–610 nm.

and reach blood vessels making the visualization possible. Upper limit would be in the frontier of visible to infrared light, that is, 760 nm. Orange and red colours fall inside the range of these wavelengths, however, the results between both of them differ. Whereas with red wavelengths (620–670 nm, Fig. 6. 5a, 5b, 5c) the illumination reaches further horizontal areas, facilitating to follow the veins direction, with orange ones (590–610 nm, Fig. 6. 4a, 4b) a better contrast is achieved and therefore more structures are visible, Fig. 7.

WGN20S3 device was implemented to show that although there exists an absorption peak in 590 nm, green light cannot penetrate the epidermis layer, hence, no visualization is achieved. It is important to highlight that WGN20S3 is the device with the highest luminous intensity (10.000 mcd). From this point, we discarded devices and light sources with a wavelength under 580 nm.

Luminosity

Only LED's with enough luminous intensity (commercially known as Ultra-bright LEDs) are able to achieve a homogeneous illumination inside the field of view (FOV) of the device. The FOV must be completely illuminated, hence, larger FOV will require higher luminous intensity. Without a uniformly illumination vessels will not be correctly distinguished, so that, luminosity is a critical parameter in a transillumination veins visualization system.

We tested LED diodes in a range of 150 to 15.000 mcd, those with enough intensity can be seen in Fig. 6, 1-5 a, b. Considering the FOV of our designed device (27 mm) good visualization results appear from 4.000 mcd, so only, Ultra-bright LEDs were used. However, in some cases, good visualization is achieved with fewer millicandelas (Fig. 6, 5c). Furthermore, increasing the intensity over a value, in our case 7.000 mcd, does not seem to be related with better results.

Angle

The light source angle must ensure a uniform illumination. LED diodes with a very small angle < 15° will illuminate isolated areas, in a spot way, creating black holes in the centre of the FOV and avoiding the visualization. However, wide angles (Fig. 6. 6a, 6b) do not focus enough the light. Fig. 8 shows the importance of a good angle selection. Whereas the left device, WON11S5, angle is 15° and the light pattern follows an isolate distribution, the right prototype illumination distribution is homogeneous due to its higher angle (30°), WCN20S3.

Common commercial LED angle range is 30°–60°, which is perfectly valid for this kind of applications.

Results

Results are split into two categories depending on the study purpose:

1) To evaluate the light source parameters, under the best light conditions, in a dark environment.
2) To evaluate the performance of the devices under real conditions, in a well illuminated environment, under different skin tones in

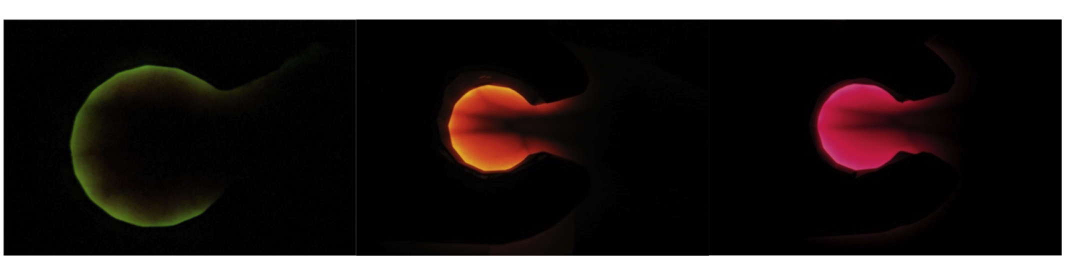

Fig. 7. Green, orange and red forearm illumination differences with devices: WGN20S3, WON20S3, WRN20S3. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

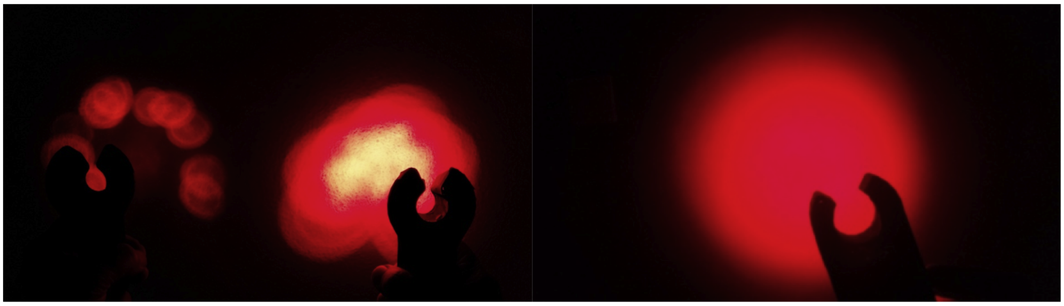

Fig. 8. Importance of the light source angle. WON11S5, WRN11S5 and WCN20S3 devices.

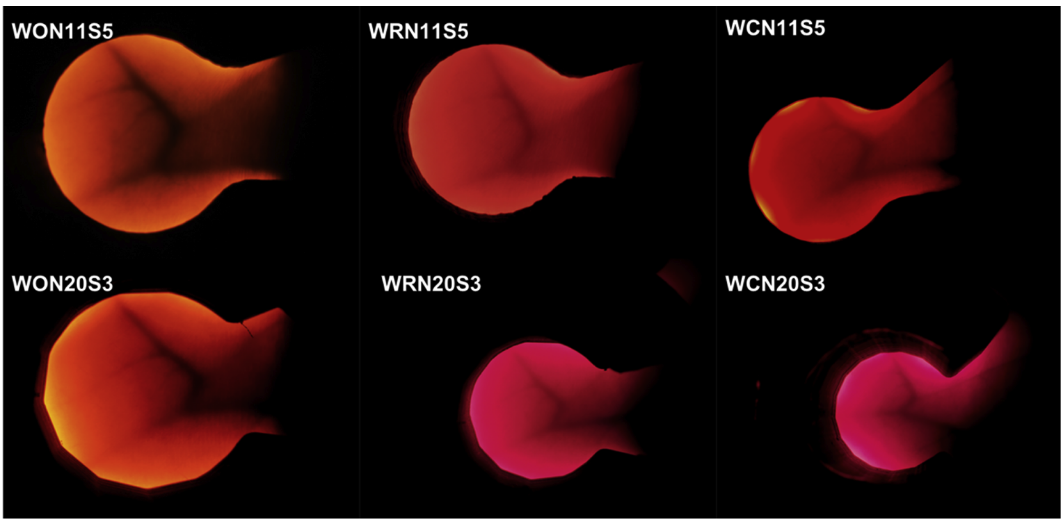

Fig. 9. Left forearm of a young woman.

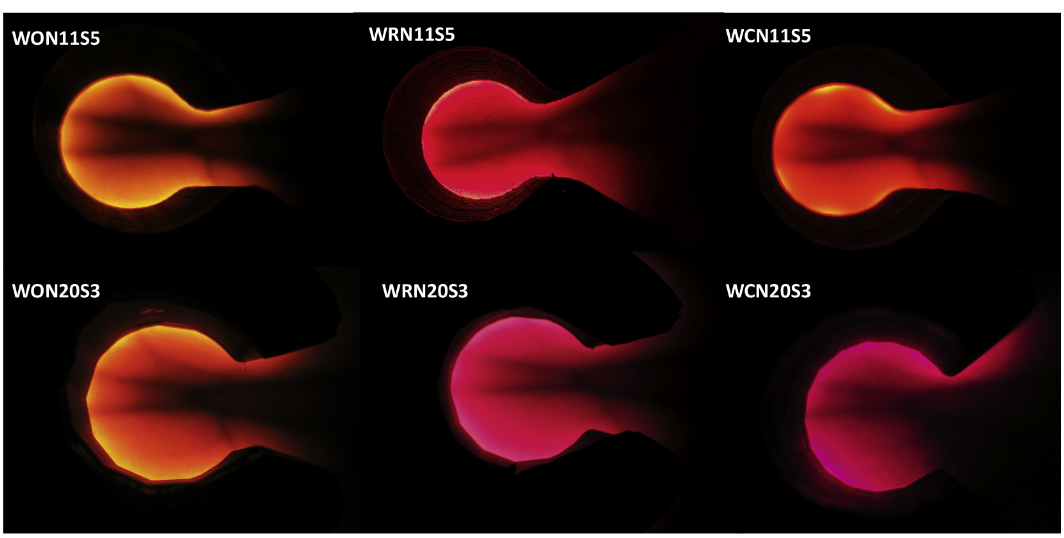

Fig. 10. Left forearm of a young man.

volunteers with different ethnic background.

Evaluation of the light source parameters

Pictures from different anatomical vessels were taken and processed to show the performance of each device under ideal conditions, in a dark environment. Together with wavelength, luminosity and angle,- parameters related to the device structure such as the number of light sources, polychromatic lights and size of the light source were studied. To begin with, the required number of light sources depends directly on the length of the FOV and inversely to the luminous intensity and the angle. We have not seen practical differences by increasing the LEDs number from 11 (WON11S5, WRN11S5, WCN11S5) to 20 (WON20S3, WRN20S3, WCN20S3), Fig. 9.

Also, the LEDs size (3 mm vs 5 mm) does not seem to take part in a better visualization. As happened with the number of light sources,

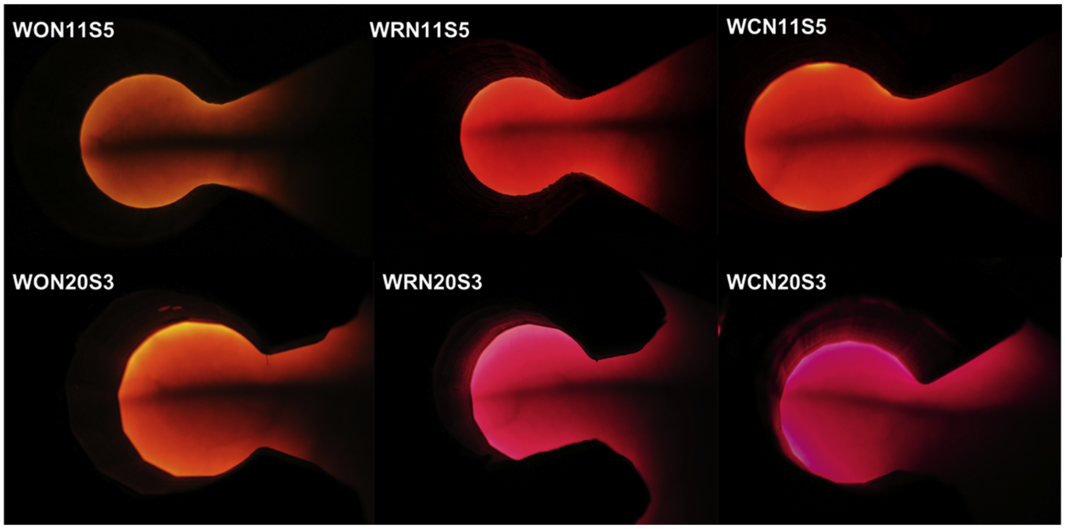

Fig. 11. Left forearm of a young woman.

diodes must ensure a uniform light distribution, no matter the size. LED's front was not studied in this work.

When studying the benefits of using polychromatic light sources, this is, using in the same device LEDs with different wavelengths, we appreciate that results do not differ or improve the results achieved with monochromatic devices. For instance, in Fig. 10, device WCN11S5 visualization is akin to WON11S5 and WCN20S3 is very similar to WON20S3 and WRN20S3 devices.

The light sources distribution, this is, the sequence of consecutive diodes with different colour, does not seem to be involved in a better visualization: For instance, in Fig. 11, device WCN11S5 sequence is 1:1 (red-orange), while the sequence of WCN20S3 device is arbitrary. No differences at a glance are found.

Experimentally, better visualization results are achieved with WON20S3, the orange device with more diodes, due to its better contrast Figs. 9, 10. However, in Fig. 11 the results among all devices are almost the same. Isolate and big vessels are found with all of them, however, little and tortuous structures are better found with wavelengths among 590–610 nm.

An image processing analysis based on histogram features was carried out under MATLAB®. Images in Fig. 10 were firstly turned to a grayscale intensity image. Afterwards, a contrast-limited adaptive histogram equalization and filtering processes were done. Fig. 12 shows the result.

Histogram images taken from the different vein finder devices are similar, with a homogeneous peak distribution. However, as we concluded before, some structures are visually enhanced when orange colour is presented in the vein finder device, both in an isolate way, as also combined with other wavelengths.

Performance of the devices in real conditions

Since medical procedures are usually done in well-light environment, the performance of the devices was also studied in those conditions, Fig. 13.

Analyses were run under a total of eight volunteers ($n = 8$). Table 3 outlines the different demographical and physiological volunteers' (*V.*) features:

Volunteers were split into groups of two individuals to evaluate different demographical and physiological features.

Pure orange devices (WON11S5 and WON20S3) provide the best results in *group 1*. Moreover, devices which use more diodes (WON20S3, WRN20S3 and WCN20S3) are better than those with less diodes (WON11S5, WRN11S5 and WCN11S5). Veins are easily found, independently of the device employed under light conditions, and can be tracked along the whole arm. No visualization differences are appreciated in these Mediterranean volunteers of different gender, age and weight.

The main difference of individuals in the second group is the age. Blood vessels are harder to be found on *V. 3* in well-light environments than on *V. 4*. In fact, only a small portion of them are seen and cannot be followed along the whole arm. As occurred with *V.1* and *V. 2,* the performance of orange devices is greater than the performance of red devices. WCN20S3 device is more effective than WRN11S5, WCN11S5 and WRN20S3. On the other hand, vessels from *V. 4*, an elderly man, are appreciated with all devices although there exist differences between red pure devices and orange ones. Again, WON20S3 evidences better results.

Differences between a normal weight and an obese individual are considered in the third group. Only the most superficial area of the vessels is visualized when applying devices with eleven diodes to *V. 5*. However, WON20S3, WRN20S3 and WCN20S3 devices shows correctly the vessels of the wrist. No greater differences are found between WON20S3*,* and WRN20S3*,* as occurred with other volunteers. On its behalf, visualization results obtained in *V. 6* are similar to those obtained in the first group. Devices with twenty LEDs perform better, and superficial veins can be tracked in the whole forearm.

Devices do not work on the Asian volunteer, *V.7* as well as on the other volunteers. Although, device WON20S3 gives a glimpse of small vessels portions, the major part of these remain hidden. No practical differences are found between WRN11S5 and WRN20S3, and between WCN11S5 and WCN20S3. Conversely, blood vessels from the dark skin volunteer, *V. 8,* are easily found with all devices. In this case, luminous intensity from the incident light source is the most critical parameter (rather than the wavelength), since vessel's contour are perfectly identified when using devices with twenty diodes.

Conclusions

Outcome images from the different evaluated devices, with different wavelengths, are very similar among them in ideal conditions. It seems that there is a better-contrast trend in tortuous vein structures when orange light (600–610 nm) is employed. Other optical parameters such as the angle or the luminous intensity will be involved in the device performance visualization regardless the employed wavelength. Based on our results, any device with a wavelength between 585 and 670 nm, an angle between 15 and 35° and a luminous intensity of 4000 mcd (or higher) which covers the whole FOV will ensure a better vein

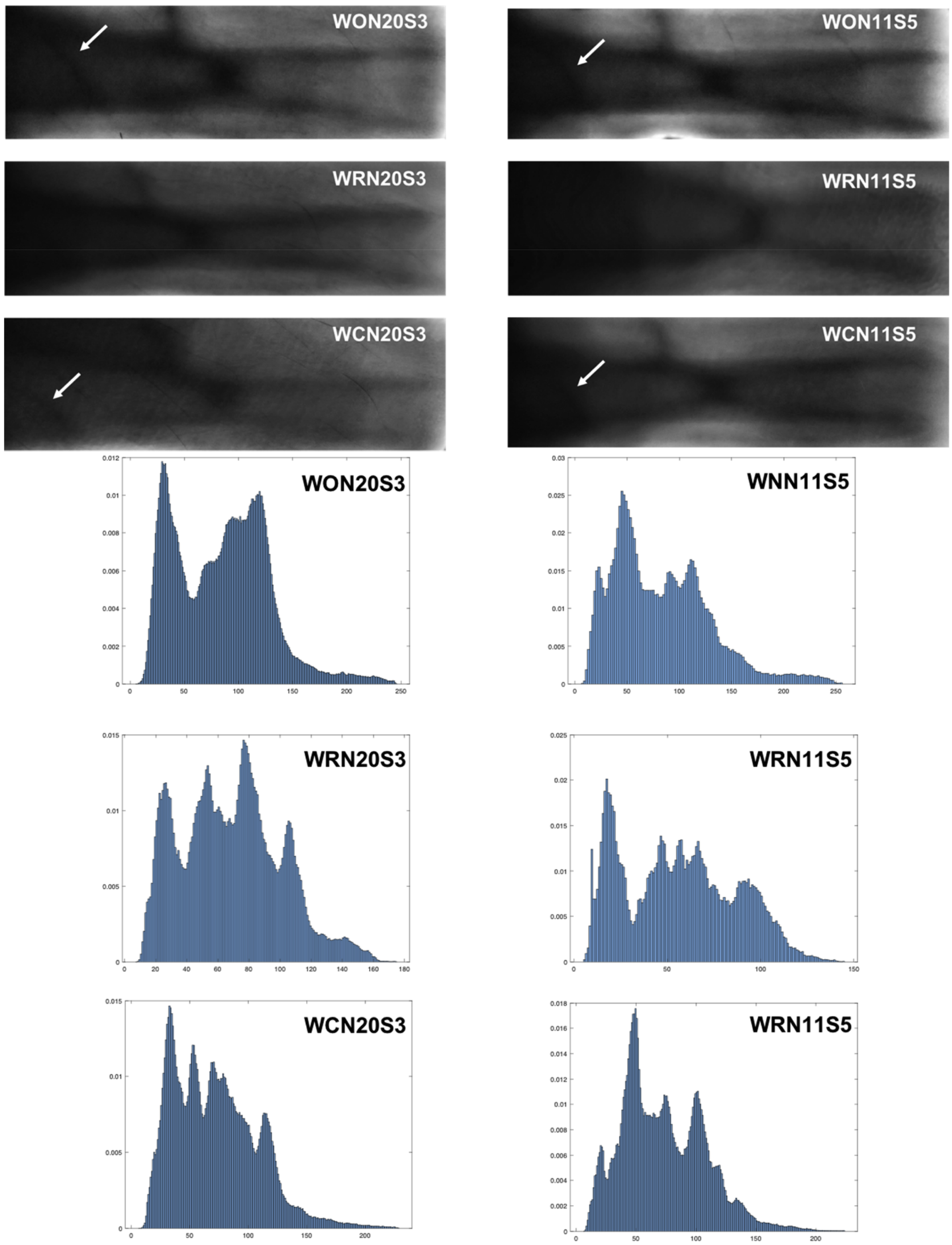

Fig. 12. Image processing results with their normalized histograms.

visualization.

The performance of the devices in real conditions vary among volunteers. Overall, WON20S3 is the best device for visualizing vessels, regardless the skin tone of the volunteer. In dark skin tones it seems that the most determinant parameter is the luminous intensity, rather than the wavelength. In very fair skin tones, like the Asian individual and the child, we found more difficulties to find large vessel sections. Differences based on other aspects like the gender do not seem to be involved in a different visualization among individuals. However, since we have studied a limited sample, further studies increasing the size of the group are required.

To conclude, results derived from this study can be useful to understand and design a biophotonic vein finder device, that can support the physician in the healthcare practice. It has been proven that these devices can be meaningful in different tasks like the non-invasive superficial veins visualization and also for obtaining a map of the veins, which, after an image processing, can be useful in the diagnosis of certain pathologies.

Acknowledgement

This work was partly supported by the Spanish MINECO under Grant TEC2015-65212-C3-2-P and TEC2017-84065-C3-1-R.

Fig. 13. Performance of WCN20S3 and WON11S5 in well-light environment in a young Mediterranean volunteer.

Table 3
Volunteers demographical and physiological features.

Volunteer	Race	Gender	Age range	Weight	Group
1	Mediterranean	Male	23	Normal	1
2	Mediterranean	Female	56	Overweight	
3	Mediterranean	Male	13	Normal	2
4	Mediterranean	Male	87	Normal	
5	South American Indian	Female	45	Class I obesity	3
6	South American Indian	Male	23	Normal	
7	Southeast Asian	Female	24	Normal	4
8	African	Male	24	Normal	

References

[1] Rivera AM, Strauss KW, van Zundert AAJ, Mortier EP. Matching the peripheral intravenous catheter to the individual patient. Acta Anæsthesiologica Belgica 2006;58(1):19.

[2] Quincy Tran. Ultrasound vs Veinviewer in Patients With Difficulty IV Access. https://clinicaltrials.gov/ct2/show/NCT02618252. Last Update Posted, January 23, 2018.

[3] Chiao FB, Resta-Flarer F, Lesser J, Ng J, Ganz A, Pino-Luey D, et al. Vein visualization: patient characteristic factors and efficacy of a new infrared vein finder technology. Br J Anaesth 2013:aet003.

[4] Guillon P, Makhloufi M, Baillie S, Roucoulet C, Dolimier E, Masquelier AM. Prospective evaluation of venous access difficulty and a near-infrared vein visualizer at four French haemophilia treatment centres. Haemophilia 2015;21(1):21–6.

[5] Ficke BW, Ransom EF, Oakes JE. Near-infrared vein visualization in index finger pollicization. Surgical Tech. 2017;42(6):481.e1–2.

[6] Zharov VP, Ferguson S, Eidt JF, Howard PC, Fink LM, Waner M. Infrared imaging of subcutaneous veins. Lasers Surg Med: The Official J Am Soc Laser Med Surg 2004;34(1):56–61.

[7] Song JH, Kim C, Yoo Y. Vein visualization using a smart phone with multispectral Wiener estimation for point-of-care applications. IEEE J Biomed Health Inf 2015;19(2):773–8.

[8] Kim D, Kim Y, Yoon S, Lee D. Preliminary study for designing a novel vein-visualizing device. Sensors 2017;17(304):1–19. https://doi.org/10.3390/s17020304.

[9] Balter ML, Chen AI, Fromholtz A, Gorshkov A, Maguire TJ, Yarmush ML. System design and development of a robotic device for automated venipuncture and diagnostic blood cell analysis. 2016 IEEE/RSJ international conference on intelligent robots and systems (IROS). IEEE; 2016. p. 514–20.

[10] Cantor-Peled G, Halak M, Ovadia-Blechman Z. Peripheral vein locating techniques. Imaging Med 2016;8(3).

[11] van Loon FHJ, Buise MP, Claassen JJF, Dierick-van Daele ATM, Bouwman ARA. Comparison of ultrasound guidance with palpation and direct visualisation for peripheral vein cannulation in adult patients: a systematic review and meta-analysis. Br J Anaesth 2018.

[12] Barreras J, Chang TP. Using a near infrared device to improve successful venous access in children with special health care needs. J Assoc Vascular Access 2017;22(2):75–80.

[13] Hosokawa K, Kato H, Kishi C, Kato Y, Shime N. Transillumination by light-emitting diode facilitates peripheral venous cannulations in infants and small children. Acta Anaesthesiol Scand 2010;54(8):957–61.

[14] Heinrichs J, Fritze Z, Klassen T, Curtis S. A systematic review and meta-analysis of new interventions for peripheral intravenous cannulation of children. Pediatr Emerg Care 2013;29(7):858–66.

[15] Haile D, Suominen PK. Technologies in pediatric vascular access: have we improved success rate in peripheral vein cannulation? Acta Anaesthesiol Scand 2017;61(7):710–3.

[16] Ross MH, Pawlina W. Histology: a text and atlas: with correlated cell and molecular biology. 6th ed.; 2011.

[17] Ash C, Dubec M, Donne K, Bashford T. Effect of wavelength and beam width on penetration in light-tissue interaction using computational methods. Lasers Med Sci 2017;32(8):1909–18.

[18] Ding H, Lu JQ, Wooden WA, Kragel PJ, Hu XH. Refractive indices of human skin tissues at eight wavelengths and estimated dispersion relations between 300 and 1600 nm. Phys Med Biol 2006;51(6):1479.

[19] Lister T, Wright PA, Chappell PH. Optical properties of human skin. J Biomed Opt 2012;17(9):090901.

[20] Tsia Kevin K. Understanding biophotonics: fundamentals, advances, and applications. Pan Stanford; 2015. p. 90.

[21] Keiser G. Biophotonics: concepts to applications. Springer; 2016.

[22] Baranoski GV, Krishnaswamy A. Light and skin interactions: simulations for computer graphics applications. Morgan Kaufmann; 2010.

[23] Fodor L et al. Aesthetic applications of intense pulsed light, 11 DOI: 10.1007/978-1-84996-456-2_2, © Springer-Verlag London Limited 2011.

[24] Instructables, A. (2017, September 28). 3d Printed Medical Vein Finder. Retrieved from http://www.instructables.com/id/3d-Printed-Medical-Vein-Finder.