



City Research Online

City St George's, University of London

Citation: Kyriacou, P. A. (2013). Direct pulse oximetry within the esophagus, on the surface of abdominal viscera, and on free flaps. *Anesthesia & Analgesia*, 117(4), pp. 824-833. doi: 10.1213/ane.0b013e3182a1bef6

This is the accepted version of the paper.

This version of the publication may differ from the final published version. To cite this item please consult the publisher's version.

Permanent repository link: <https://city-ref-test.eprints-hosting.org/id/eprint/3546/>

Link to published version: <https://doi.org/10.1213/ane.0b013e3182a1bef6>

Copyright and Reuse: Copyright and Moral Rights remain with the author(s) and/or copyright holders. Copies of full items can be used for personal research or study, educational, or not-for-profit purposes without prior permission or charge, unless otherwise indicated, provided that the authors, title and full bibliographic details are credited, a hyperlink and/or URL is given for the original metadata page and the content is not changed in any way. For full details of reuse please refer to [City Research Online policy](#).

Direct Pulse Oximetry Within the Esophagus, on the Surface of Abdominal Viscera, and on Free Flaps

Panayiotis A. Kyriacou, BSc, MSc, PhD

BACKGROUND: Pulse oximetry is a noninvasive photometric technique that provides information about arterial blood oxygen saturation (Sp_{O_2}) and heart rate and has widespread clinical applications. This is accomplished via peripheral pulse oximetry probes mainly attached to the finger, toe, or earlobe. The direct application of pulse oximetry to an organ, such as the esophagus, liver, bowel, stomach or free flap, might provide an indication of how well perfused an organ or a free flap is. Also, the placement of a pulse oximetry probe at a more central site, such as the esophagus, might be more reliable at a time when conventional peripheral pulse oximetry fails.

METHODS: The focus of this article is the development and in vivo applications of new custom-made photoplethysmographic (PPG) and pulse oximetry optical and fiberoptic probes and instrumentation in an effort to investigate their suitability for the estimation of arterial blood oxygen saturation at different organs and tissues. The article will cover examples of application areas including real-time PPG and Sp_{O_2} monitoring for the esophagus and solid organs, including free flaps, using custom-made probes.

RESULTS: Clinical studies have successfully demonstrated the feasibility of acquiring PPGs and estimating arterial blood oxygen saturation values from a variety of organs and tissues.

CONCLUSIONS: The technological developments and the measurements presented in this work pave the way to a new era of pulse oximetry where direct and continuous monitoring of blood oxygen saturation of internal organs and tissues (esophagus, bowel, liver, stomach, free flaps) could be possible.

Optical sensors and medical instrumentation, in general, have played an important role in medicine and biology for many years. Such technologies have been used extensively for monitoring, diagnostic, prognostic, or therapeutic purposes. The current advancements in semiconductor and optoelectronic technologies, including the new innovations in biosignal processing techniques, enable the developments of more intelligent miniature sensors. Such sensors are challenging the current status quo in medical monitoring as more sensors are now applied invasively or noninvasively in various anatomical parts which was not possible only a few years ago. These sensors reveal information for the first time to clinical experts which will aid in more optimized treatment of patients and in the further understanding of various pathophysiological phenomena.

The most popular optical sensor is the pulse oximeter. Pulse oximetry is clearly one of the most significant technological advances in clinical monitoring.¹⁻³ Pulse oximetry is a noninvasive photometric technique that provides information about arterial blood oxygen saturation (Sp_{O_2}) and heart rate and has widespread clinical applications. Pulse oximetry was so popular that Kelleher⁴ reviewed 220 studies

from an article published in 1989, and in a follow-up review in 1992, Severinghaus and Kelleher⁵ found more than 500 new reports between 1989 and October 1991. Nearly 12,000 more reports on pulse oximetry have been published since October 1991.

Pulse oximetry provides an indication of arterial oxygen saturation. This is accomplished via peripheral pulse oximetry probes mainly attached to the finger, toe, or earlobe. For many years, researchers have evaluated and compared pulse oximeters in different environments, conditions, and clinical cases. The technological and physiological limitations of pulse oximeters have been identified and discussed in the literature.^{6,7} Many pulse oximetry manufacturers have been actively developing and optimizing their designs, both in sensors and processing systems, to overcome some of the well-known pulse oximetry limitations (failures due to low pulsation and motion artifact, etc.), plus expand pulse oximetry technology capabilities beyond traditional arterial oxygen saturation by providing quantifying information on other blood chromophores, such as methemoglobin, carboxyhemoglobin, hemoglobin concentration, and pleth variability, to assess intravascular volume responsiveness, etc.⁸

Although pulse oximetry seems to be at the peak of its development, there is always room for further improvement, optimization, and innovation. Many of these innovations could relate to specific applications, and this will be the focus of this article. Perhaps this is the time to investigate photoplethysmographic (PPG) signals and blood oxygen saturation in different organs and tissues. The direct application of pulse oximetry to an organ such as the esophagus, liver, bowel, or other vascular tissues such as free flaps might be a very useful application in determining whether an adequate volume of arterial blood is reaching the intended vascular area. This might be important when there is concern regarding the vascularization of an organ or tissue, and it

From the School of Engineering and Mathematical Sciences, City University London, United Kingdom.

Accepted for publication June 6, 2013.

Funding: Part of this work was supported by Joint Research Board of St Bartholomew's Hospital, London, United Kingdom, and Engineering and Physical Sciences Research Council (EPSRC), United Kingdom.

The author declares no conflicts of interest.

Reprints will not be available from the author.

Address correspondence to Panayiotis A. Kyriacou, BSc, MSc, PhD, School of Engineering and Mathematical Sciences, City University London, London EC1V 0HB, United Kingdom. Address e-mail to P.Kyriacou@city.ac.uk.

can find applications during surgical interventions such as bowel resection, organ transplantation, or free flap surgery. Also, placement of a pulse oximetry probe at a more central site such as the esophagus might prove more reliable at a time when conventional peripheral pulse oximetry fails.

It is not the intention of this article to provide a review of pulse oximetry (i.e., physics, technology, applications, limitations, etc.). The focus will be the development and applications of PPG, pulse oximetry optical fiberoptic probes as well as instrumentation in an effort to investigate their suitability for the estimation of arterial blood oxygen saturation within the esophagus, on the surface of abdominal viscera, and on free flaps.

METHODS

Technological Developments

In this section, all optical sensors and instrumentation developed for the various applications will be briefly described. Technical descriptions of these technologies can be found in all relevant references more in depth.

Esophageal Pulse Oximeter

Peripheral perfusion is often poor in patients undergoing prolonged major surgery. Hence, the arterial blood oxygen saturation readings from commercial finger pulse oximeters can become unreliable or cease when they are most needed. To overcome this limitation, the esophagus has been investigated as an alternative measurement site, because perfusion may be preferentially preserved centrally. A reflectance adult optical esophageal pulse oximeter probe was fabricated⁹⁻¹¹ using 2 infrared (IR) and 2 red surface-mount emitters and a surface-mount photodetector (Fig. 1). The peak emission wavelengths of the IR and red emitters used were 880 and 655 nm, respectively. The esophageal probe was designed to fit into a 20-Fr gauge plastic transparent disposable stomach/esophageal tube (Pennine Healthcare, Derby, United Kingdom). A custom-made finger reflectance probe, optically and electronically identical to the esophageal probe, has also been developed to facilitate comparisons between the 2 sites (esophagus and finger).¹⁰ A neonatal esophageal pulse oximetry sensor was also constructed^{12,13} (dimensions: 14 × 2 mm), comprising 1 IR (880 nm) and 1



Figure 1. Adult esophageal pulse oximetry probe.

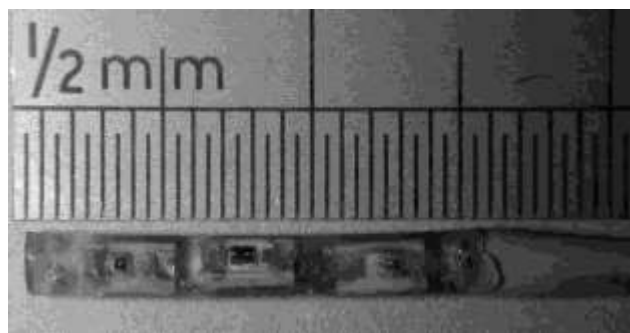


Figure 2. Close-up photo of the neonatal esophageal pulse oximetry probe.

red (655 nm) surface-mount emitter and a surface-mount 1 mm² active area photodetector (Fig. 2). The esophageal probe was designed to be small enough to slide down the lumen of a plastic transparent disposable size 12-Fr (external diameter of 3.8 mm) nasogastric tube.

Splanchnic Pulse Oximetry Probe

A hand-held fiberoptic probe (Fig. 3) was designed for placement in the abdominal cavity, during open laparotomy, on both hollow and solid organs.¹⁴ Fiberoptic cables were chosen as a means of transmitting and receiving the light because they are electrically safe and their dimension (cross-sectional area) can be quite small so as to ultimately facilitate insertion of the sensor into a small cavity. Glass



Figure 3. Splanchnic pulse oximetry fiberoptic probe.

silica step index multimode fibers with a numerical aperture of 0.37 and a core diameter of 600 μm were used, with each fiber cable SubMiniature version A (SMA) terminated at 1 end. Two optical fibers were coupled to red and IR SMA-mounted emitters (with peak emission wavelengths of 650 and 850 nm, respectively), and the third fiber was coupled to an SMA-mounted photodiode (1 mm² active area). To facilitate the multiplexing of the red and IR signals into a single fiber, a 400-nm bifurcated fiber (or Y-piece) from Ocean Optics (Ocean Optics, Duiven, The Netherlands) was used. To compare the PPG signals, acquired from abdominal organs when using the fiberoptic sensor, an identical (with the same optical and electrical characteristics) peripheral fiberoptic PPG/Spo₂ probe has also been developed.

Free Flap Pulse Oximetry Probe

Accurate and continuous monitoring of free flap survival in reconstructive plastic microsurgery (e.g., after plastic surgery for reconstructing the breast after mastectomy due to breast cancer) and early identification of flap failure are vital for flap salvage. The success of such procedures depends strongly on the maintenance of adequate oxygen in the flap. Early diagnosis of ischemia and surgical exploration to restore blood flow can often salvage the flap and may prevent graft failure. Therefore, there is a need for a monitoring technique that is continuous, noninvasive, accurate, easy to use, reproducible, and inexpensive. A reflectance pulse oximetry probe for placement on free flaps¹⁵ after plastic microsurgery (adult patients) has been developed (Fig. 4). The geometry and dimensions of the probe were determined by considering the physical characteristics and geometry of free flaps (with a focus on deep inferior epigastric perforator [DIEP] free flaps). The main optical components of the probe were mounted on a copper-clad kapton sheet (DuPont, Wilmington, DE) to provide a flexible printed circuit board base that can be set into a semi-flexible probe using optically clear epoxy-resin (DYMAX Corporation, Torrington, CT). This type of fabrication allows flexibility in the probe to accommodate the curvature of the free flap and to electrically isolate the probe components when they come into contact with the skin. Three



Figure 4. Free flap pulse oximetry probe.

light-emitting diodes (LEDs) of different wavelengths were chosen for the probe construction: 660 nm red, 940 nm near-IR, and 520 nm green. The first 2 LEDs are traditional wavelengths used in pulse oximetry systems and can therefore be used to estimate Spo₂. The green LED has a relatively short penetration depth and therefore will enable the investigation of PPGs in the free flap immediately beneath the probe. The photodetector was a surface-mount photodiode with peak sensitivity at 940 nm, with enhanced sensitivity down to the blue end of the optical spectrum.

Processing and Data Acquisition System

A pulse oximetry processing system was constructed to preprocess, record, and display PPG signals and estimate Spo₂ values on a laptop personal computer. Various versions of the processing system⁹⁻¹⁴ have been developed within the Biomedical Research Laboratory at City University London over the years. Because they all share many similarities, a standard PPG/Spo₂ platform has been recently developed to accommodate all pulse oximetry probes (custom-made and commercial). The new research pulse oximetry processing system is named ZenPPG. The ZenPPG is a dual channel, dual wavelength PPG system, which combines the advantages of standardization of instrumentation, compatibility with commercial probes, and the ability to customize the system for specific projects. The main parts of the system are a system bus, PPG modules (current supplies, probe connector board, and transimpedance amplifiers), and power supply conditioning board. All the modules were designed to be as simple as possible allowing incremental improvement during subsequent development of the system. The completed ZenPPG system is shown in Figure 5. The PPG signals at the



Figure 5. ZenPPG pulse oximetry processing system. The top photograph shows the front panel of the completed (all electronics are enclosed) 2-channel pulse oximetry system. The bottom photograph shows the printed circuit boards of the dual channel pulse oximetry system.

output of the ZenPPG system were digitized (1000 samples per second) by a 16-bit data acquisition card on a laptop personal computer. The digitized PPG signals were further analyzed by data acquisition software named LabVIEW (National Instruments Corporation, Austin, TX). The developed software reads all acquired PPG data, converts them into a spreadsheet format and saves them into a file specified by the user, and displays the PPG signals at all wavelengths in real time on the screen of the laptop computer. Algorithms were also developed for the online estimation of SpO_2 .

Clinical Studies

This section will describe the various in vivo investigations performed using the aforementioned pulse oximeter probes.

Clinical Investigation 1: Esophageal PPG Signals and Blood Oxygen Saturation Measurements in Cardiothoracic Surgery Adult Patients

This study investigated and compared esophageal and finger PPGs and SpO_2 s in patients undergoing high-risk operations, such as hypothermic cardiothoracic bypass surgery, in whom conventional pulse oximetry might fail due to poor peripheral circulation.^{9,16–18} After receiving ethics approval and written patient consent, 50 adult patients were recruited for this study.¹⁷ Having previously found^{9,18} that PPG signals in the midesophagus (20–25 cm from the upper lip) are of large amplitude, the esophageal pulse oximeter probe was advanced into the esophagus at 30 cm from the lips after induction of anesthesia. PPG signals were observed at various depths in the esophagus until the site that provided the best quality (high signal-to-noise ratio) PPG signals was determined. During the esophageal measurements, blood oxygen saturation values from a commercial transmission finger pulse oximeter (Marquette, Tram 200A; Marquette Electronics, Milwaukee, WI) were also recorded. Monitoring with the esophageal pulse oximeter was performed intermittently¹⁷ during the various periods of the operation (during induction of anesthesia, before commencing cardiopulmonary bypass, after bypass, and postoperatively in the intensive care unit). During the aforementioned recording periods, samples of arterial blood were taken and analyzed by an Instrumentation Laboratories IL BG-1400 Blood Gas Analyzer (BGA) (Instrumentation Laboratories, Lexington, MA). Simultaneous SpO_2 measurements were also recorded from the custom-made finger probe and a commercial finger pulse oximeter.

Clinical Investigation 2: Esophageal PPG Signals and Blood Oxygen Saturation Measurements in Neonates

Local research ethics committee approval and written consent were obtained for this proof-of-concept pilot study.¹³ Five neonates (3 male, 2 female) were studied in the neonatal and pediatric intensive care units. The age range (days, $\pm$ SD) was (5–1398, $\pm$ 606), and the weight range (kg, $\pm$ SD) was (1.9–10.0, $\pm$ 3.3). The esophageal SpO_2 probe was advanced gently through the mouth to a maximum depth of about 15 cm from the lips. The babies' lungs were mechanically ventilated, and the babies adequately sedated. The probe was withdrawn slowly, and PPG signals were observed at various depths to determine the optimal measuring site at which reliable PPG signals (high signal-to-noise ratio) were obtained. The probe was then left at this depth for the duration of the study for approximately

10 minutes, and PPG traces and SpO_2 values were recorded simultaneously. Esophageal measurement of blood oxygen saturation values, from a commercial toe pulse oximeter (Datex Ohmeda Biox 3740, GE Healthcare, Buckinghamshire, UK) with disposable Datex Ohmeda toe sensor (Oxytip Allfit sensor, OXY-AF, Datex Ohmeda, GE Healthcare, Helsinki, Finland), was also recorded for comparison.

Clinical Investigation 3: Investigation of PPG Signals and Blood Oxygen Saturation from Various Abdominal Organs

Local research ethics committee approval was obtained to investigate ASA physical status I and II patients undergoing elective laparotomy after they gave informed written consent.^{19–22} PPG measurements were made in 17 patients, (3 male and 14 female, mean age [$\pm$ SD]: 54 [$\pm$ 9.7] years), undergoing open laparotomy. All patients were tracheally intubated, and their lungs mechanically ventilated. The fiberoptic pulse oximetry probe was placed into a sterile transparent medical ultrasound cover. When the abdominal cavity was open, the surgeon placed the splanchnic pulse oximeter probe on the surface of each accessible abdominal organ (bowel, liver, etc.). PPG signals were acquired for approximately 2 minutes on each site. For comparison purposes, the identical fiberoptic finger pulse oximeter probe was placed on the index finger of the right hand. Blood oxygen saturation from a commercial finger pulse oximeter (GE Healthcare, Buckinghamshire, United Kingdom) placed on the middle finger of the right hand was also recorded.

Clinical Investigation 4: Investigation of PPG Signals and Blood Oxygen Saturation in DIEPs Free Flaps

Pilot clinical investigations were performed to evaluate the functionality of the PPG probe in 10 patients (mean age [$\pm$ SD]: 54.8 [$\pm$ 9.4] years) undergoing elective breast reconstruction with DIEP flap. This study was approved by the local research ethics committee, and the patients' consent was obtained before recruitment. After the breast reconstructive surgery, the PPG probe was taped (Transpore, 3M) onto the exposed skin of the flap, and postoperative PPG/ SpO_2 measurements were obtained intermittently every 15 minutes in the first 2 hours, every 30 minutes for the following 4 hours, and hourly for the next 12 hours. Patient vital signs such as heart rate, arterial blood pressure, SpO_2 , and temperature were recorded in conjunction with keeping a record of the clinical observations of the free flap performed by the clinical team, that is, color, temperature, capillary refill, and pinprick test results.

RESULTS

Results from the Investigation of Esophageal PPGs and SpO_2 s in Cardiothoracic Surgery Adult Patients

Measurable PPG traces at both wavelengths were obtained in the esophagus of all patients. Figure 6 depicts typical traces from 1 patient undergoing cardiopulmonary bypass surgery during the various monitoring periods as described earlier (monitoring depth at 17 cm). Figure 6A shows esophageal and finger AC PPGs, obtained at both wavelengths, and electrocardiogram signals recorded just before sternotomy. Figure 6B shows PPG and electrocardiogram signals after bypass in the intensive care unit, respectively.

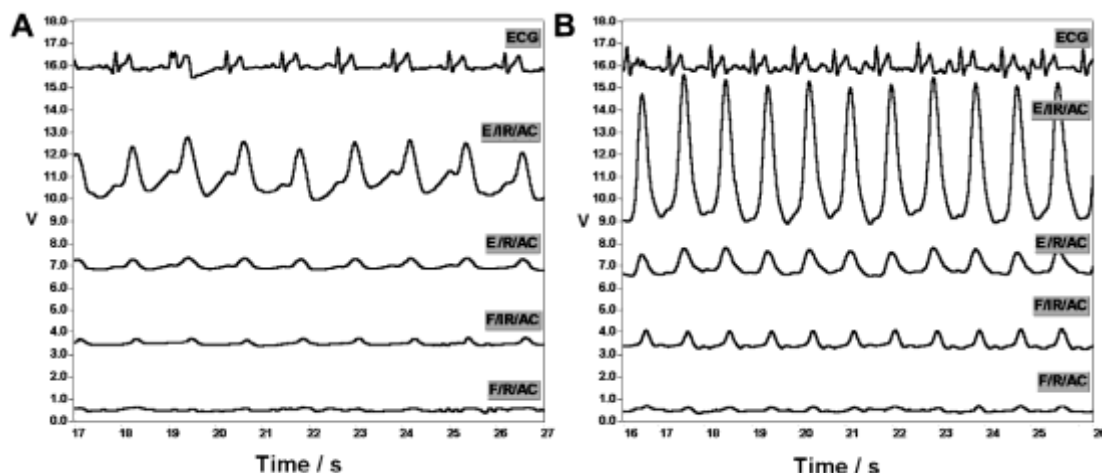


Figure 6. Esophageal (E), Finger (F), photoplethysmographic (PPG), and electrocardiogram traces obtained from an anesthetized patient undergoing cardiopulmonary bypass surgery; (A) in operating room before sternotomy; (B) postoperatively in the intensive care unit. ECG = electrocardiogram; IR = infrared.

Table 1. Mean $\pm$ SE of AC Peak-to-Peak Photoplethysmographic (PPG) Amplitudes (mV) at 2 Wavelengths Measured in the Upper, Mid, and Lower Esophagus

Esophageal depths	Mean AC PPG amplitudes (mV)		
	Upper esophagus (14–17 cm)	Midesophagus (18–22 cm)	Lower esophagus (27–28 cm)
Infrared (880 nm)	177 $\pm$ 18 mV	532 $\pm$ 72 mV	358 $\pm$ 42 mV
Red (655 nm)	69 $\pm$ 7 mV	222 $\pm$ 29 mV	183 $\pm$ 37 mV
No. of patients (n)	27	19	4

The esophageal PPG signals recorded from all patients (before and after bypass) were of good quality with large amplitudes. Monitoring esophageal depth ranged from 14 to 28 cm, measured from the upper lip (mean $\pm$ SD: 17.8 $\pm$ 3.3 cm). Optimal esophageal monitoring depth for each patient was considered the depth with esophageal PPGs with good signal-to-noise ratios. Table 1 gives the mean $\pm$ SE of the AC PPG amplitudes at both wavelengths at the different esophageal monitoring depths for the 50 patients. The amplitudes at the monitoring depths as described in Table 1 were separated into 3 groups: the upper esophageal depths (14–17 cm), the midesophageal depths (18–22 cm), and the lower esophageal depths (27–28 cm). The AC PPGs in the mid to lower esophagus (depths of 18 cm or more) had larger mean amplitudes at both wavelengths than those in the upper esophagus (14–17 cm).

In a direct comparison of blood oxygen saturation measurements from the esophagus and values from the BGA, 155 sets of blood oxygen saturation values from 50 patients were used for regression analysis, which gave the estimated slope and intercept of the regression line. An average ($\pm$ SD) of 3.5 ($\pm$ 1.5) blood samples was collected from each patient. The range of all BGA results was 92.7% to 100% with a mean of 98.5% and a standard deviation of 1.6%. A plot of Spo_2 readings obtained from the reflectance esophageal pulse oximeter (y-axis) and the BGA (x-axis) is shown in Figure 7. The equation of the best fit linear regression line was: $y = 12.3 + 0.88x$; $r = 0.86$; standard error of estimate = 0.86; $P < 0.001$. The mean and standard deviation for the differences between the esophageal pulse oximeter and blood gases were $0.02\% \pm 0.88\%$.

A regression analysis of the ratio of ratios (R) as measured by the esophageal pulse oximeter versus the BGA

oxygen saturation values is shown in Figure 8. The equation of the best fit linear regression line was: $\text{Spo}_2 = 108.2 - 21.1 \times (R)$; $r = 0.86$; standard error of estimate = 0.84; $P < 0.001$. The dashed line represents the empirical calibration equation ($\text{Spo}_2 = 110 - 25 \times [R]$) used for the estimation of esophageal Spo_2 . The equation derived from the regression analysis of the ratio of ratios as measured by the esophageal pulse oximeter versus BGA ($\text{Spo}_2 = 108.2 - 21.1 \times [R]$ [solid line in Fig. 8]) shows that there is close agreement between the 2 equations. This new esophageal calibration equation can replace the empirical calibration equation ($\text{Spo}_2 = 110 - [R] \times 25$) in the data acquisition algorithm for estimating esophageal Spo_2 . The new calibration equation would result in esophageal Spo_2 values closer to the BGA.

Table 2 summarizes the results of the regression analysis between Spo_2 values obtained from the 3 pulse oximeters (esophageal, custom-made finger, and commercial finger) and arterial oxygen saturation (Sao_2) values obtained from BGA. Of the 50 patients included in the study, 5 patients (10%) had 1 or more periods of at least 10 consecutive minutes, during which the commercial and custom-made finger pulse oximeters failed to record pulsatile PPG signals and display Spo_2 values, despite being correctly positioned on the finger. The esophageal pulse oximeter operated successfully throughout these periods of finger monitoring failure. In 4 of these patients, the finger pulse oximeter failed postoperatively in the intensive care unit (within the first half hour after completion of the surgery), and in the fifth patient, the failure occurred in the operating room before bypass. Results from arterial blood gas analysis performed during these periods of failed finger pulse oximetry demonstrate good agreement (mean difference = 0.0%) between

Figure 7. Comparison of arterial blood oxygen saturation (Sp_{O_2}) measurements obtained from the esophageal probe (y-axis) and the blood gas analyzer (x-axis) in 49 patients; the solid line represents the best fit linear regression line. $y = 12.3 + 0.88x$; $r = 0.86$; standard error of estimate = 0.86; $n = 155$; $P < 0.001$. The dashed line represents identity. The error bars represent esophageal Sp_{O_2} error of $\pm 0.8\%$. Sa_{O_2} = arterial oxygen saturation.

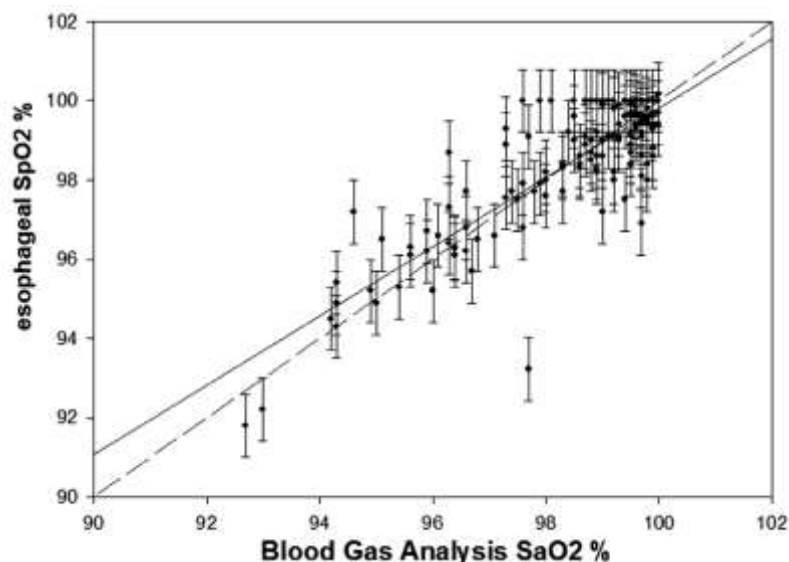


Figure 8. Comparison of the blood gas analyzer (y-axis) and the ratio of ratios measured by the esophageal pulse oximeter (x-axis) in 49 patients. The solid line represents the best fit linear regression line. $y = 108.2 - 21.1x$; $r = 0.86$; standard error of estimate = 0.84; $n = 155$; $P < 0.001$. The dashed line represents the empirical calibration equation ($y = 110 - 25x$) used for the estimation of esophageal arterial blood oxygen saturation (Sp_{O_2}). R/IR = red/infrared.

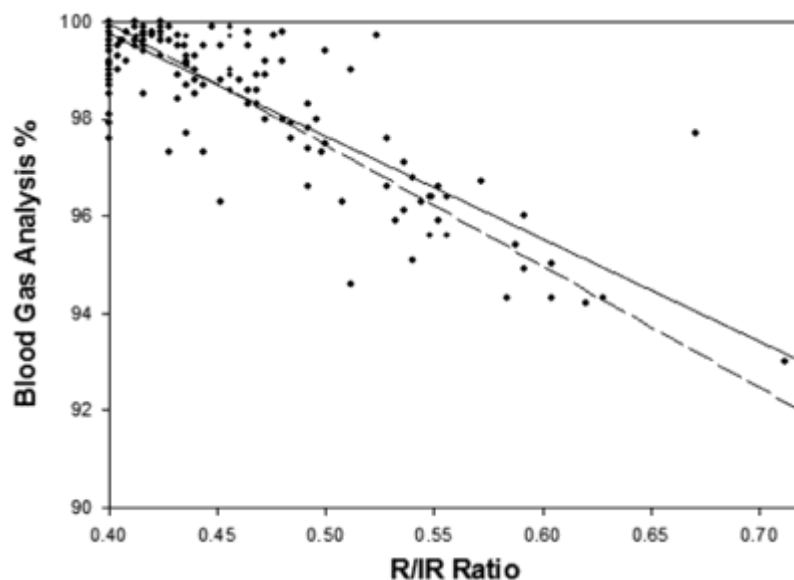


Table 2. Calculated Values of the Relationships Between Sp_{O_2} And Sa_{O_2} Obtained from Blood Gas Analysis (BGA) for the Esophageal, Custom-Made Finger, and Commercial Finger Pulse Oximeters

	Esophageal versus BGA	Custom-made finger versus BGA	Commercial finger versus BGA
Mean difference ($\pm$ SD)	$0.002\% \pm 0.88\%$	$0.19\% \pm 1.24\%$	$0.33\% \pm 1.54\%$
Standard error of estimate	0.86%	1.09%	1.48%
Correlation coefficient (r)	0.86	0.69	0.63

Sp_{O_2} = arterial blood oxygen saturation; Sa_{O_2} = arterial oxygen saturation.

the oxygen saturation values obtained from the esophageal pulse oximeter and the BGA.

Results from the Investigation of Esophageal PPG Signals and Sp_{O_2} s in Neonates

In this pilot study, good quality PPG signals from the esophagus were recorded in all patients. The measured effective signal-to-noise ratio was always better than 40 dB at the output of the system. A Bland and Altman^{23,24} test was performed to compare the 2 pulse oximeters (esophageal and

toe). The result of this test will show whether the 2 methods can be used interchangeably.

Eighteen pairs of Sp_{O_2} values from the 5 patients were used to compare the esophageal and commercial toe pulse oximeters. Calculations of the bias, estimated by the mean difference (d), and the standard deviation of the differences (s) were performed to assess the degree of agreement between the 2 methods. The bias (d) is the esophageal pulse oximeter (ES) reading minus the commercial toe (CT) pulse oximeter reading ($ES - CT$) and was +0.34% with a standard

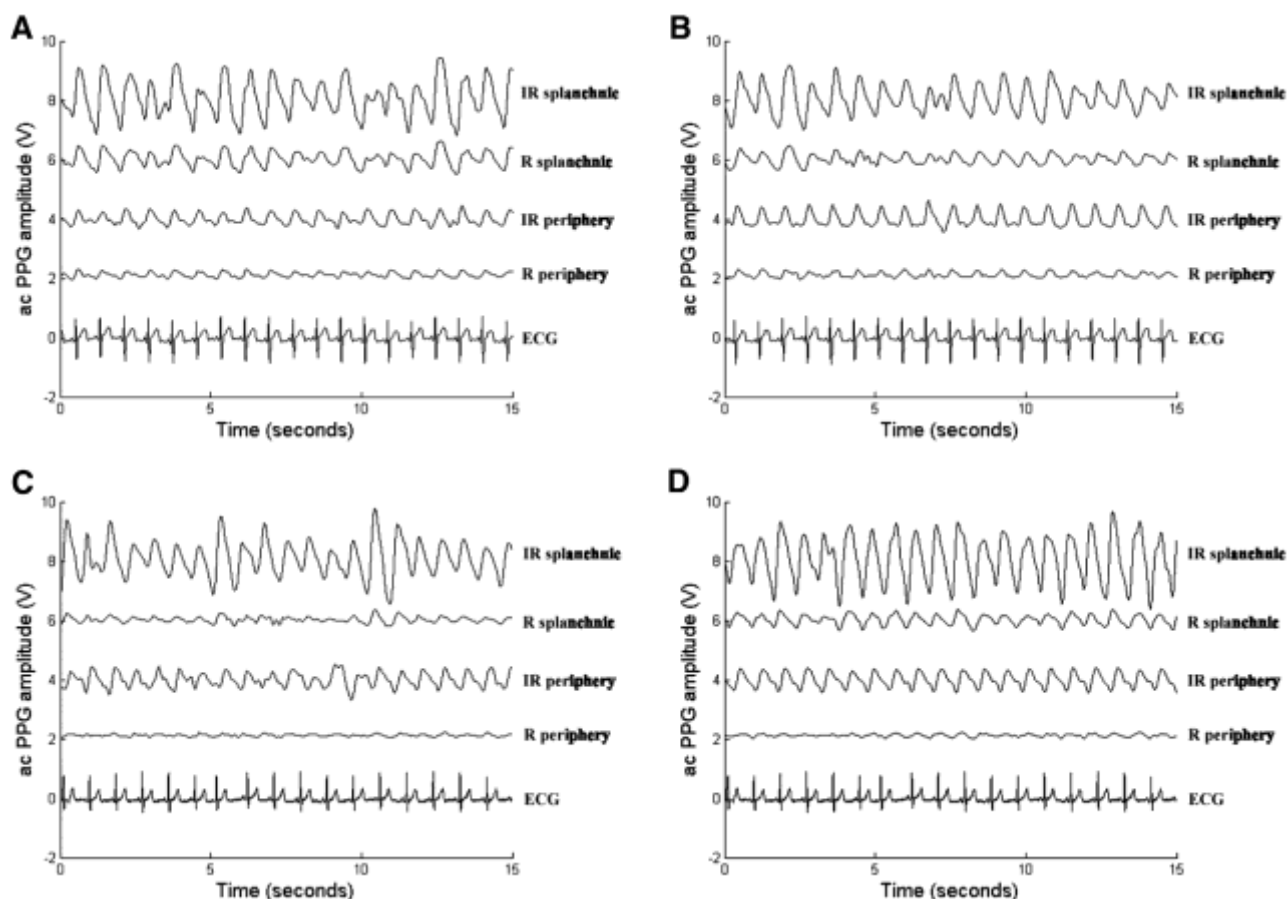


Figure 9. AC red (R) and infrared (IR) photoplethysmographic (PPG) signals from the (A) small bowel, (B) large bowel, (C) liver, and (D) stomach. All splanchnic PPGs are accompanied by a finger PPG. ECG = electrocardiogram.

deviation (s) of 0.67%. Hence, the limits of agreement for the SpO_2 data (ES and CT) were -1.00% and $+1.70\%$.

Results from the Investigation of PPG Signals and SpO_2 s from Various Abdominal Organs

Good quality PPG signals with large amplitudes were recorded in all attempts from the small bowel ($n = 17$), large bowel ($n = 14$), liver ($n = 5$), and stomach ($n = 5$). Figure 9 depicts red and IR PPG traces from the small and large bowel, liver, stomach, and the finger. The low-frequency artifact present on the splanchnic PPG traces was due to the mechanical ventilator and movement of the hand-held sensor. Table 3 shows the mean AC PPG amplitudes for each investigated organ including the finger.

Although this is an uncalibrated pulse oximetry system, preliminary SpO_2 values were calculated for the small bowel, large bowel, liver, stomach, and finger. Table 4 presents the results from the Bland and Altman analysis of these data.

Table 3. Mean ($\pm$ SD) Infrared (IR) and Red (R) AC photoplethysmographic (PPG) Amplitudes for All Sites

Site	Mean IR AC (V)	Mean R AC (V)
Small bowel ($n = 17$)	2.37 ± 1.26	0.76 ± 0.41
Large bowel ($n = 14$)	2.29 ± 1.11	0.76 ± 0.35
Liver ($n = 5$)	3.32 ± 2.47	0.91 ± 0.82
Stomach ($n = 5$)	1.71 ± 0.84	0.62 ± 0.23
Finger ($n = 17$)	0.85 ± 0.26	0.23 ± 0.07

Results from the Investigation of PPG Signals and SpO_2 s in DIEP Free Flaps

PPG signals at all 3 wavelengths were recorded in the post-operative period from all patients (excluding 1 patient where green PPGs were not available). Figure 10 depicts typical PPG signals from one of the DIEP flaps, together with

Table 4. Bland and Altman Test Results (Comparing the Custom-Made Pulse Oximeter [Applied to Various Organs] with a Commercial Finger Pulse Oximeter)

	Mean difference (%) $\pm$ SD	d - 2s (%)	d + 2s (%)
Commercial finger pulse oximeter versus small bowel pulse oximeter ($n = 17$)	0.6 ± 3	-5.41	6.59
Commercial finger pulse oximeter versus large bowel pulse oximeter ($n = 14$)	0.7 ± 2.8	-4.91	6.33
Commercial finger pulse oximeter versus liver pulse oximeter ($n = 5$)	-3.2 ± 2.6	-8.37	1.97
Commercial finger pulse oximeter versus stomach pulse oximeter ($n = 5$)	2 ± 4.5	-7.1	11.1

d = mean difference; s = standard deviation.

Figure 10. Deep inferior epigastric perforator (DIEP) and finger AC photoplethysmographs (PPG) at 3 wavelengths.

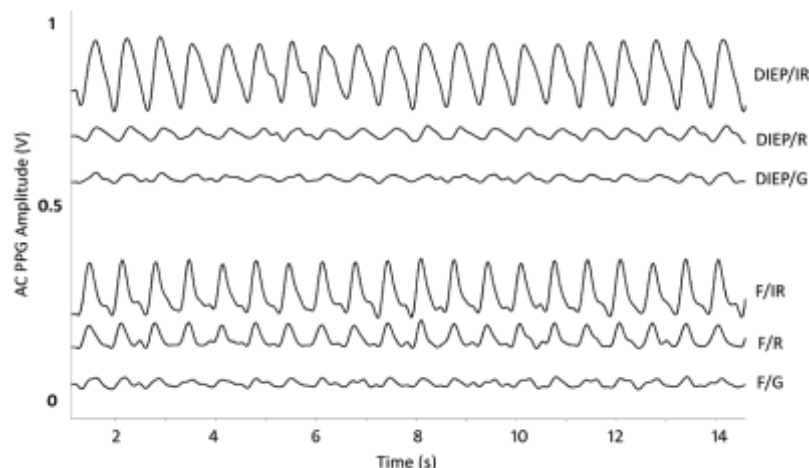
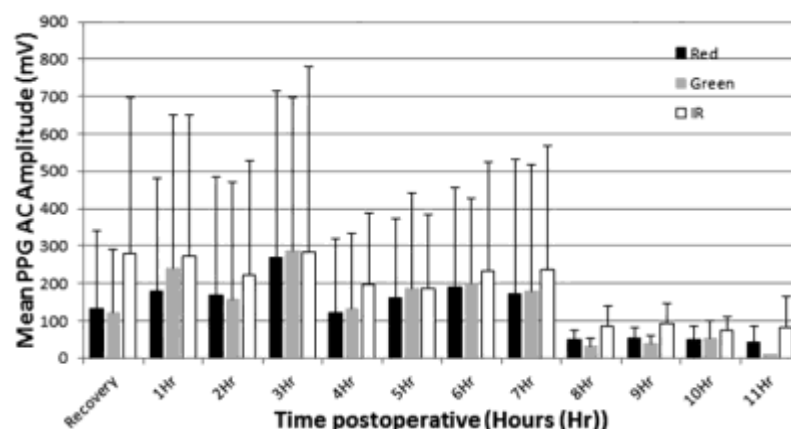


Figure 11. Mean ($\pm$ SD) AC photoplethysmograph (PPG) amplitudes at 3 wavelengths from the deep inferior epigastric perforator flaps of all 10 patients during the postoperative period. IR = infrared.



simultaneous PPG recordings from an identical finger probe, obtained at 2 hours into the postoperative period. Figure 11 shows a preliminary PPG amplitude analysis of all 10 subjects. In this figure, the mean ($\pm$ SD) PPG amplitudes, at 3 wavelengths as recorded in the different monitoring times are presented. Preliminary free flap blood oxygen saturation values were estimated using the red and IR PPGs to calculate the ratio of ratios and then use a linear equation ($\text{Spo}_2 = 110 - 25R$) to calculate Spo_2 s. Because this is an uncalibrated system, the estimated free flap blood oxygen saturation values were consistently lower than the Spo_2 values from the commercial finger pulse oximeter. A comparison of the 2 pulse oximeters (free flap and finger) was performed using Bland and Altman^{23,24} test (see Fig. 12). Seventy-seven pairs of Spo_2 values from the 10 patients were used to compare the free flap and the commercial finger pulse oximeters.

The mean difference (d) was -13.3% and the standard deviation (s) was 13.2% . The limits of agreement were:

$$\begin{aligned} d - 2s &= -0.2 - (2 \times 1.0) = -39.6\% \\ d + 2s &= -0.2 + (2 \times 1.0) = 13.2\% \end{aligned}$$

DISCUSSION

Pulse oximetry is a noninvasive photometric technique that provides information about Spo_2 and has widespread clinical applications. Currently, pulse oximetry uses peripheral probes which are mainly attached to the finger, toe, or earlobe. Despite its success as an indicator of arterial oxygen

saturation, there is a need to explore pulse oximetry as a technique that can be applied to other parts of the body such as internal organs and other tissues. The monitoring

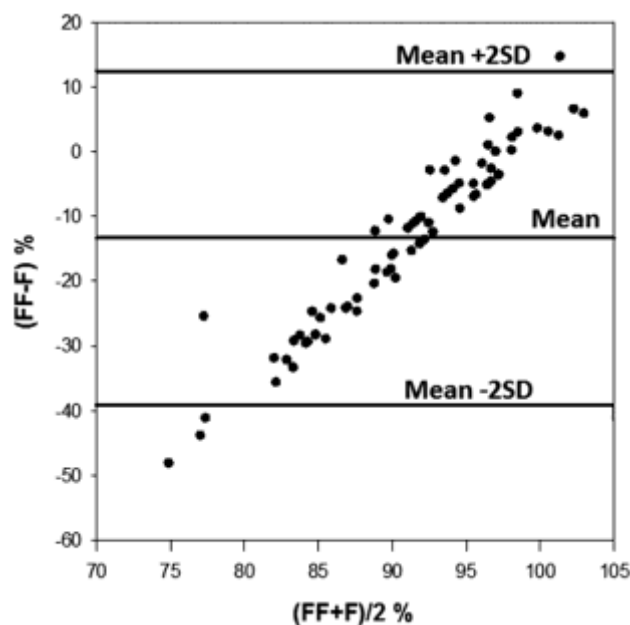


Figure 12. Difference against mean for arterial blood oxygen saturation (Spo_2) data obtained from the free flap (FF) and the finger (F) pulse oximeters.

of SpO_2 of other more central organs, such as the esophagus, might be useful at times when conventional pulse oximetry fails to estimate correct SpO_2 values from more peripheral sites such as the finger. This could be accomplished with the design of new pulse oximetry probes having the capability to attach to specific organs or tissues.

A miniature optoelectronic reflectance esophageal (adult) oximeter probe small enough to fit into a conventional stomach tube (20-Fr gauge) was developed. The results show that the esophageal probe can record good quality red and IR, AC, and DC PPG signals from any depth within the esophagus. This probe allows optimization of the signal by variation of the monitoring depth and is therefore more versatile than the previously described "transesophageal" probe²⁵⁻²⁸ that could only be positioned in the upper esophagus at the cricopharyngeus muscle. The SpO_2 results from the esophageal pulse oximeter were in good agreement with blood oxygen saturation values obtained from BGA. The esophageal pulse oximeter was reliable and accurate in cases of poor peripheral circulation when the commercial finger pulse oximeter failed for at least 10 minutes. Five (10%) of the 50 cardiothoracic patients studied had a finger pulse oximetry failure, which is in agreement with previously reported incidences of failure.²⁹ Although the percentage failure rate in this study was only approximately 10% in terms of absolute numbers, this would be a significant clinical problem and a reliable means of monitoring throughout such a failure would be of real value. These results show that, in cardiothoracic patients, arterial blood circulation to the esophagus is less subject to vasoconstriction and decreased PPG amplitudes than the finger. Therefore, the human esophagus can be used as an alternative SpO_2 monitoring site during surgery and in intensive care. Moreover, these results suggest that the esophagus will continue to provide reliable SpO_2 values even when peripheral pulse oximeters fail. Only 5 patients showed peripheral failure in this study and, therefore, more work is needed to confirm these findings in cardiothoracic and other patients. The recorded esophageal PPG signals from all neonates were of high quality, and in a direct comparison between the esophageal pulse oximeter and a commercial toe pulse oximeter, using Bland and Altman analysis, the preliminary SpO_2 results from the 2 instruments were in good agreement. This pilot study supports the initial hypothesis that the esophagus may be used as an alternative measuring site for SpO_2 in neonates and children. It appears to be the first report of the calculation of SpO_2 values from PPG signals recorded in the neonatal esophagus.

The new hand-held fiberoptic splanchnic pulse oximeter probe recorded good quality PPG signals and provided SpO_2 estimates with $\pm 4\%$ accuracy from various abdominal organs. The fiberoptic pulse oximetry system in its current hand-held design could be a useful tool for surgeons, enabling the assessment of some surgical outcomes early, such as the quality of surgical anastomosis. However, the main limitation of the study was that it did not allow for assessment of the device on patients with compromised bowel or other splanchnic organ perfusion. As a result, all SpO_2 values were within the normal range. The data range of the results presented may be too narrow for Bland and

Altman analysis to be helpful in assessing interchangeability of methods. Therefore, the next step in evaluating the system would be to conduct more rigorous clinical investigations on a group of patients in whom splanchnic perfusion is compromised.

The multiwavelength PPG free flap sensor was successfully used in monitoring PPGs and SpO_2 values during free flap (DIEP) reconstructive surgery. Good quality PPG signals from the free flaps were acquired during the intraoperative and postoperative period. This appears to be the first time that a multiwavelength PPG system has been used for simultaneous monitoring of PPGs in flaps. There have been some studies of free flap perfusion (animals or humans) using PPG systems.^{30,31} The majority of these studies have not investigated or presented DIEP flap PPGs and SpO_2 s from the intraoperative to the postoperative stages. The main effort of most of these studies was to detect arterial or venous occlusion by deliberately clamping the vessels intraoperatively. Also, the majority of the previous attempts used PPG sensors that were not custom made for such applications. Despite the initial success in monitoring free flap PPGs and estimating arterial blood oxygen saturation values, these preliminary results showed that the saturation values were low in the majority of the cases when compared with a commercial finger pulse oximeter. This might have been due to either the uncalibrated nature of the custom-made pulse oximeter or due to low or weak free flap PPG pulsations which is one of the limitations of the technique of pulse oximetry which could result in erroneous estimation of SpO_2 . It is conceivable that the loss of an adequate PPG signal over these flaps could serve as an early warning of impaired perfusion, but confirmation of this must await further studies.

In summary, this article reviewed new custom-made pulse oximetry probes that were designed and fabricated for placement on various organs and tissues. The clinical studies successfully demonstrated the feasibility of acquiring PPGs and estimating blood oxygen saturation values from a variety of organs and tissues. The technological developments and the measurements presented in this work pave the way to a new era of pulse oximetry where direct and continuous monitoring of blood oxygen saturation of internal organs and tissues could be made possible. **E**

REFERENCES

1. Alexander CM, Teller LE, Gross JB. Principles of pulse oximetry: theoretical and practical considerations. *Anesth Analg* 1989;68:368-76
2. Tremper KK, Barker SJ. Pulse oximetry. *Anesthesiology* 1989;70:98-108
3. Welch J. Pulse oximeters. *Biomed Instrum Technol* 2005; 39:125-30
4. Kelleher JF. Pulse oximetry. *J Clin Monit* 1989;5:37-62
5. Severinghaus JW, Kelleher JF. Recent developments in pulse oximetry. *Anesthesiology* 1992;76:1018-38

6. McMorrow RC, Mythen MG. Pulse oximetry. *Curr Opin Crit Care* 2006;12:269–71
7. Webster JG. Design of Pulse Oximeters. 1st ed. Bristol, UK: IOP Publishing, 1997
8. Shamir MY, Avramovich A, Smaka T. The current status of continuous noninvasive measurement of total, carboxy, and methemoglobin concentration. *Anesth Analg* 2012;114:972–8
9. Kyriacou PA. Pulse oximetry in the oesophagus. *Physiol Meas* 2006;27:R1–35
10. Kyriacou PA, Moye AR, Gregg A, Choi DM, Langford RM, Jones DP. A system for investigating oesophageal photoplethysmographic signals in anaesthetised patients. *Med Biol Eng Comput* 1999;37:639–43
11. Kyriacou PA, Powell S, Langford RM, Jones DP. Esophageal pulse oximetry utilizing reflectance photoplethysmography. *IEEE Trans Biomed Eng* 2002;49:1360–8
12. Kyriacou PA, Jones DP, Langford RM, Petros AJ. Pilot study in neonatal and paediatric oesophageal pulse oximetry. *Anesth Analg* 2007;105:S106–S107
13. Kyriacou PA, Jones DP, Langford RM, Petros AJ. A pilot study of neonatal and pediatric esophageal pulse oximetry. *Anesth Analg* 2008;107:905–8
14. Hickey M, Samuels N, Randive N, Langford RM, Kyriacou PA. Measurement of splanchnic photoplethysmographic signals using a new reflectance fiber optic sensor. *J Biomed Opt* 2010;15:027012
15. Zaman T, Kyriacou PA, Pal SK. Development of a reflectance photoplethysmographic sensor used for the assessment of free flap perfusion. *Conf Proc IEEE Eng Med Biol Soc* 2011;2011:4006–9
16. Kyriacou PA, Powell S, Langford RM, Jones DP. Investigation of oesophageal photoplethysmographic signals and blood oxygen saturation measurements in cardiothoracic surgery patients. *Physiol Meas* 2002;23:533–45
17. Kyriacou PA, Powell SL, Jones DP, Langford RM. Evaluation of oesophageal pulse oximetry in patients undergoing cardiothoracic surgery. *Anaesthesia* 2003;58:422–7
18. Kyriacou PA, Moye AR, Choi DM, Langford RM, Jones DP. Investigation of the human oesophagus as a new monitoring site for blood oxygen saturation. *Physiol Meas* 2001;22:223–32
19. Hickey M, Kyriacou PA, Samuels N, Randive N, Chang SH, Maney KM, Langford RM. Photoplethysmographic signals recorded from human abdominal organs using a fibre-optic probe. *Br J Anaesth* 2009;102:579–80
20. Hickey M, Samuels N, Randive N, Langford RM, Kyriacou PA. An *in vivo* investigation of photoplethysmographic signals and preliminary pulse oximetry estimation from the bowel using a new fiberoptic sensor. *Anesth Analg* 2011;112:1104–9
21. Hickey M, Samuels N, Randive N, Langford RM, Kyriacou PA. Investigation of photoplethysmographic signals and blood oxygen saturation values obtained from human splanchnic organs using a fiber optic sensor. *J Clin Monit Comput* 2011;25:245–55
22. Hickey M, Samuels N, Randive N, Langford RM, Kyriacou PA. A new fibre optic pulse oximeter probe for monitoring splanchnic organ arterial blood oxygen saturation. *Comput Methods Programs Biomed* 2012;108:883–8
23. Altman DG, Bland JM. Measurement in medicine: the analysis of method comparison studies. *The Statistician* 1983;32:307–17
24. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986;1:307–10
25. Atlee JL, Bratanow N. Comparison of surface and esophageal oximetry in man. *Anesthesiology* 1995;83:A455
26. Prielipp RC, Scuderi PE, Butterworth JF, Royster RL, Atlee JL. Comparison of transesophageal pulse oximetry (TEPO) with peripheral surface pulse oximetry in CABG patients. *Anesthesiology* 1996;85(3A):A485
27. Borum SE. The successful use of transesophageal pulse oximetry in a patient in whom peripheral pulse oximetry was unobtainable. *Anesth Analg* 1997;85:514–6
28. Prielipp RC, Scuderi PE, Hines MH, Atlee JL, Butterworth JF. Comparison of a prototype esophageal oximetry probe with two conventional digital pulse oximetry monitors in aortocoronary bypass patients. *J Clin Monit Comput* 2000;16:201–9
29. Reich DL, Timcenko A, Bodian CA, Kraidin J, Hofman J, DePerio M, Konstadt SN, Kurki T, Eisenkraft JB. Predictors of pulse oximetry data failure. *Anesthesiology* 1996;84:859–64
30. Lindsey LA, Watson JD, Quaba AA. Pulse oximetry in post-operative monitoring of free muscle flaps. *Br J Plast Surg* 1991;44:27–9
31. Futran ND, Gal TJ, Farwell DG. Radial forearm free flap. *Oral Maxillofac Surg Clin North Am* 2003;15:577–91