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A compact instrument to measure perfusion of vasculature in transplanted maxillofacial free flaps

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Abstract

The vascularization and resulting perfusion of transferred tissues are critical to the success of grafts in buried free flap transplantations. To enable long-term clinical monitoring of grafted tissue perfusion during neovascularization and endothelialization, we are developing an implantable instrument for the continuous monitoring of perfusion using diffuse correlation spectroscopy (DCS), and augmented with diffuse reflectance spectroscopy (DRS). This work discusses instrument construction, integration, and preliminary results using a porcine graft model.

Keywords

Perfusion monitoring; Microcirculation; Diffuse correlation spectroscopy; Diffuse reflectance spectroscopy; Maxillofacial transplantation; Buried free flap; Implantable optical monitoring; Continuous perfusion monitoring

1. INTRODUCTION

Facial injuries due to trauma can involve massive damage and avulsion to tissues central to complex systems responsible for seeing, hearing, smelling, breathing, eating, and talking. The potential psychological impact due to disfigurement as well as the proximity to vital structures in the head and neck region renders maxillofacial injuries potentially devastating to health and emotional well-being.

Free tissue transfer is the current standard for the reconstruction of injured and missing tissue throughout the body. Because maxillofacial injuries can be complex and can involve the skin and soft-tissues as well as bones resulting in fractures, the complexity of tissue transplant is significantly increased in these cases.

After free tissue transfer, flap perfusion is maintained only by anastomosed circulation until endothelialization occurs across the anastomotic line (typically around 2 weeks). Prior to

endothelialization the risk of flap failure is the highest, and early warning of flap failure is critical to salvage via re-exploration or pharmacological means.

Anywhere from 5 to 25% of free flaps necessitate re-exploration due to circulatory compromise, with salvage rates reported as 44.9%.^[1] The majority of microvascular thrombi occur within the first 2 or 3 postoperative days. In general, venous compromise was more common than arterial compromise, with reported figures ranging from 54 to 63% of thrombosed vessels.^[2] Venous thrombosis is also more common during the first 3 to 5 days postoperatively. Arterial compromise, conversely, is less common and tends to occur after 1 week.

Conventional free flap monitoring techniques (clinical observation, hand-held Doppler ultrasonography, surface temperature probes, and pinprick testing) are all existing methods for monitoring free flaps with an external component. Buried free flaps lack an external component; thus, conventional monitoring is limited to hand-held Doppler ultrasonography. Free flap success is enhanced by the rapid identification and salvage of failing flaps. There is no currently accepted method of flap monitoring ideal for use in all types of free tissue transfers, and none provide objective, easily communicated data.^[3,4]

Unrecognized venous thrombosis or compromise from extrinsic compression can progress rapidly to arterial thrombosis and ultimate flap failure. In jejunal flaps, it has been found that if circulation to a failing flap is not reestablished within 8 to 12 hours, salvage may become impossible, and initial blood flow results in hyperemia followed by a gradual decline in perfusion. Reperfusion injury also commonly leads to cellular death and necrosis.

The implantable Doppler probe has been used with success in head and neck reconstruction, though it suffers from a lack of specificity.⁵

Continuous monitoring of tissue-oxygen partial pressure (ptiO_2) has been reported using the implantable Licox probe (Integral Life Sciences, Plainsboro, NJ), however the flap can only be monitored in one location and there is no additional flow data, only oxygen saturation, limiting the clinical specificity for suggesting interventions.

Another technique of flap monitoring in the head and neck using laser Doppler flowmetry in combination with spectrophotometry has been reported. Unfortunately, laser Doppler is unable to monitor anything deeper than superficial tissue, whereas DCS is able to produce signals from deeper tissues. In our lab, DCS is used routinely at 50 mm depth, more than enough to monitor buried free flaps, and possibly enough to provide diagnostic value without any invasive component.

2. MATERIALS AND METHODS

2.1 Diffuse Correlation Spectroscopy for the monitoring of microvascular perfusion

Diffuse correlation spectroscopy (DCS) is an optical technique which enables quantifying relative changes in microvascular blood flow (rBF). DCS uses coherent near-infrared light to penetrate tissue, while a detector measures speckle fluctuations in scattered diffuse light. The speckle signal is modulated in time by the collective motion of all scatterers in the

tissue, though there is a wide range of time scales over which signal modulated by moving red blood cells dominate the power spectrum.

The DCS signal is the normalized intensity autocorrelation, $g_2(\tau)$, of the time series of detection events. The autocorrelation is calculated with a multi-tau method (Magatti & Ferri, 2001). The normalized intensity autocorrelation function for single-scattering is (Yu, Durduran, Zhou, Cheng, & Yodh, 2011):

$$g_2(\tau) = \frac{\langle I(t)I(t+\tau) \rangle}{\langle I(t) \rangle^2} \quad \text{Equation 1}$$

where τ is the lag time after t , t is time and I is the intensity of detected light. The extension to multiple-scattering is detailed in [6]. The autocorrelation function calculated by the DCS system integrates the effect of all scattering events within the interrogation volume. In addition to the movement of the scattering particles, the autocorrelation signal also contains information about the optical properties of the tissue. The optical properties related to the autocorrelation signal are include the absorption coefficient, μ_a , the reduced scattering coefficient, μ'_s , the fraction of moving scatterers, α , and the mean square displacement of scatterers, $\langle r^2(\tau) \rangle$. This results from the fact that the autocorrelation can be thought to diffuse through the tissue in a similar way as the photons diffusing through the tissue.

With a single mode collection fiber placed at some distance from the illumination fiber, the probability distribution of photons migrating from source to detector fibers form what is known as a “banana pattern”, allowing for interrogation of tissues at controlled depth.

The key components of a DCS flow-meter include a long-coherence length laser at NIR range, a single-photon-counting avalanche photodiode (APD) detector and an autocorrelator. Other components, such as source/detector fibers, computer, and A/D board, are used to couple light in/out of tissue or control/record optical data. For tissue blood flow measurement, the laser placed on the tissue surface (e.g., skin) launches long-coherence NIR light into the tissue via a multiple-mode source fiber, and the light transported/scattered through the tissue was collected by a single-mode (or a few-mode) detector fiber placed millimeters to centimeters away from the source fiber. The detected light is then delivered via the detection fiber to the APD detector, where the count of photons per unit time (i.e., light intensity) is recorded. The temporal fluctuation of light intensity in a single speckle area of tissue collected by the detector fiber is associated with the motion of moving scatterers (primarily red blood cells in microvasculature) and can be quantified by calculating the decay of the light intensity autocorrelation function using the autocorrelator. Because the absolute value of blood flow index (αD_B) is affected by many factors (e.g., the coupling between fiber and tissue surface) and varies across subjects, most of studies only reported the relative change in blood flow (rBF) during or post physiological manipulation as compared to the baseline (before physiological manipulation).

The use of DCS for the study of blood flow has been pioneered by the laboratory of Dr. Arjun Yodh at the University of Pennsylvania [7, 8, 9]. Several subsequent papers have

demonstrated and continue to demonstrate the utility of DCS for various biomedical applications. These studies include: Duduran (2009) [10] which used DCS to monitor cerebrovascular hemodynamics in acute stroke patients, Buckley et al. (2009) [11] which used DCS to monitor cerebral hemodynamics in premature infants undergoing positional intervention, and Zhou et al. (2009) [12] which monitored cerebral hemodynamics in piglet brains following head injury.

DCS provides a portable, noninvasive, and inexpensive alternative for microvascular blood flow measurements and has been validated against other standards, including power spectral Doppler ultrasound, laser Doppler flowmetry, Xenon computed tomography, fluorescent microsphere flow measurement, and ASL-MRI. The DCS technology has been extensively introduced into various tissues, including brain, tumor and skeletal muscle.

2.2 Diffuse Reflectance Spectroscopy (DRS) to measure tissue oxygenation

An important sign of well-perfused tissue is its vascular oxygenation, which can directly be measured by DRS. It is also possible to use DRS for determination of the tissue scattering and absorption coefficients (μ_s and μ_a respectively), knowledge of which improves the modeling and therefore the accuracy of DCS measurements. Light propagation in biological tissue is dependent on the absorption and scattering coefficients within the tissue medium, where these properties themselves depend upon both the biochemical composition as well as the morphological composition of tissue [13, 14]. Measurements of diffuse reflectance (or transmittance) spectra involve detection of multiply scattered light through the tissue and can be quantitatively analyzed using rigorous light-tissue interaction models to extract the absorption and scattering properties of tissues.

Blood oxygen saturation is measured by DRS as a result of obtaining quantitative estimates of the oxy-, deoxy-, and total hemoglobin concentrations using the tissue absorption coefficient. Measurement of vascular oxygenation using DRS differs from the arterial SpO_2 measured using pulse oximetry. In pulse oximetry, tissue absorption is determined using the AC or pulsatile portion of the transmitted intensity of light at two pre-selected wavelengths. Tissue absorption is estimated to be dependent only on the oxy- and deoxy- hemoglobin concentrations, which in turn allows calculation of the arterial saturation. There is no rigorous analysis to account for tissue geometry, presence of other tissue chromophores or for tissue scattering in pulse-oximetry. Calculation of vascular oxygenation using DRS, on the other hand, involves measurement of the reflectance spectrum using a broadband light source. The measured reflectance or transmitted spectrum is analytically computed using a light-tissue interaction model (an inverse Monte Carlo model, in our case) and then matched to the experimental measurements to derive these wavelength dependent absorption and scattering coefficients. The extracted absorption coefficient allows us to compute the relative amounts of oxygenated and deoxygenated hemoglobin present in the sensed volume.

2.3 DCS instrumentation at RMD

The RMD Perfusion Monitor is a 2-channel diffuse correlation spectroscopy (DCS) system with integrated diffuse reflectance spectroscopy (DRS) capabilities (Figure 3). The hardware

is contained within a single box, having SMA and FC fiber terminations in the front panel for both illumination and detection. 8 channel systems are also available in larger form factor.

DCS requires a laser source with a long coherence length. It is important that the scattering volume is smaller than the coherence volume of the incident radiation.[15] In other words the coherence length of the source must be longer than the width of the distribution of detected photon path lengths through the scattering medium such that all detected photons will interfere coherently. We have found that relatively inexpensive diode lasers (Thorlabs LD785-SH300) have coherence lengths sufficient for DCS in human tissue. The DRS source is a wide bandwidth white LED, and all sources are driven in constant-current mode. The light is delivered through a step index optical fiber (Thorlabs FG200LEA) with a core diameter of 200 μm . The scattered light is collected by a single-mode fiber (Thorlabs 780HP with a 4.4 μm core diameter). Software for the DCS system, including laser control and data saving routine, is currently integrated into a single software package, while software for DRS spectral collection currently resides in a separate application.

2.4 Correlator

2 channels of intensity autocorrelation are collected by a single custom-made PSoC time-tagger and USB data logger. Multiple PSoC boards can be driven by a master board to enable 4 channels of data collection per USB connection. The maximum speed of the correlator is determined by the integration time of 80ns enabled by the PSoC clock, resulting in a correlation plot with a maximum resolution of .08 μs . The maximum data rate is approximately 150kHz per channel, as limited by USB transfer. Alternate architectures which preserve the low cost of the PSoC design may push this to MHz in future iterations.

A software suite has been written in C#, allowing full control of the instrument from a GUI (Figure 4), and enabling 4 channels of DCS data to be collected simultaneously. DRS data collection is automated as well. Raw photon time data and calculated correlation plots can be stored simultaneously and continuously with no upper time limit.

The correlation algorithm is based upon the multi-tau method, [16] with all calculation currently being performed on the CPU of the computer controlling the instrument. At this time, real time correlation analysis is possible with 800 ns maximum timing resolutions (4 channels at 50kHz/ch), while increasing the resolution to 80 ns results in 10 s of the same data requiring ~120 s to complete through the correlation algorithm. Alternate algorithms are currently in beta testing to decrease the software load. [17] The maximum resolution of the correlation algorithm (and the resulting CPU load) can be adjusted for real-time analysis, allowing for raw data to be automatically analyzed at higher resolution *ex-post facto*. Correlation can also be disabled for high rate raw data collection.

Further details on the correlator and GUI are available in Stapels, *et al.* [18]

2.5 DCS probes

The probes utilized in this work fall into the two categories of non-invasive skin probes and biocompatible implantable probes for continuous direct monitoring of the vein, artery, and capillary flow in the graft.

Skin probes—Fiber-coupled silicone slab probes are described in detail in Farkas, et al. [19] Briefly, the probes consist of fiber optic illumination fibers (200 μm multimode) and 4 single mode collection fibers at source-detector fiber spacings 1, 2, 5, and 10 mm. Fibers to enable DRS (200 μm delivery and 105 μm collection) were also included. The fibers are fixed in an epoxy chuck (Hysol 9460, Loctite corp.) at precise spacings and normal to the skin. This chuck is encased in a silicone slab (Sylgard 186, Dow Chemical) which provides adhesion as well as protection and strain relief to the fibers, which are jacketed in black furcation tubing and terminated with SMA and FC ferrules.

Implantable probes—Fiber-coupled miniature probes are being developed at RMD to allow post-surgical monitoring of free flaps. In a manner similar to the commercial Cook-Schwarz Doppler probe, the fibers will be removable after successful graft acceptance (typically several weeks after surgery). They will attach to both the pedicle as well as the flap itself, with the methods of securing them being bioresorbable or inert. Prior to our planned long-term implantation trials, short-term implantation trials can utilize prototypes which are completely removable.

One delivery and one collection fiber were encased again in Hysol 9460 epoxy, with ~ 1 mm spacing between them. Two versions of the low profile probe were made, which are depicted in Figure 6:

Angled fiber with aramid garrote: A probe was created by first encasing fibers at precise spacings in Hysol 9460 via a follicle-shaped mold, then sanding and polishing the fibers/epoxy at an angle of 60° . This assembly was then bonded to silicone-encased aramid strings via UV cured adhesive. The entire assembly was then encased in a thin layers of medical grade silicone. Throughput from this device was approximately 1/10 that of the silicone slab skin probes at similar spacings.

Right angle (RA) prism coupled fiber with PTFE collar: Fibers were coupled to miniature RA prism ($200 \times 200 \times 200$ μm) via UV-cured adhesive. The assembly was then encased in Hysol 9460, threaded into a PTFE collar similar in scale to that used by the commercial Cook-Swartz RF Doppler probe. The entire assembly was encased in a thin layer of medical grade silicone. Throughput from this device was similar to the angled fiber probe.

2.6 Free flap failure in an animal model

A porcine model for free flap transplantation was utilized to evaluate the utility of the instrument. The pedicle (blood carrying arterial and venous supply) was variably clamped to simulate full blood flow vs. fully occluded/clamped while our instrument monitored blood flow conditions at several sites on the flap and pedicle. All studies were performed at

University of Michigan aided by our collaborators. The studies were also performed with the aid of our collaborators in the Biomedical Engineering department at University of Michigan.

15 Kg (~ 1 week old) pigs were initially anesthetized with Telazol. Anesthesia was maintained with isoflurane and the pigs were tracheally intubated. Intravenous fluids, 0.9 normal saline were given at a maintenance rate throughout the procedure.

As a model for a maxillofacial free flap, a latissimus Dorsi flap based on the thoracodorsal artery was raised with an approximately 5×5 cm skin paddle. The arterial and venous supply was traced back to the subclavian artery and vein removing all branches so that a single vascular supply and drainage exists for study purposes. 100% oxygen with isoflurane mixture was delivered to the pig before and during the procedure. O₂ SAT was measured using standard pulse oximetry on the flap directly prior to and at several points during the experiment.

Probes were determined to be operating in accordance with expectations on both solid phantoms and using human transdermal “thumb” trials, and laser power levels were set to maximize signal after placement on the flap.

Three probes were attached to the free flap and artery, and a Hoffman type screw clamp was utilized on the arterial side to vary blood flow to the flap. DCS data were collected continuously, with 10 second integration times, before, during, and after clamping for a total of 600 seconds. DRS data files, with 3 averages of 1 second integrations, were collected before, during, and after clamping. DCS plots were re-processed at the maximum data resolution *ex-post facto*.

A table of clamping/flow observations was compiled, and a pseudo-quantitative chart of clamping vs time was created to be overlayed upon our fitted DCS data:

3. RESULTS AND DISCUSSION

DCS correlation plots were simultaneously recorded from 4 locations (see Table below) on the buried free flap & pedicle while blood supply was occluded using the Hoffman screw clamp. The DCS data stream totaled 60× 10 second integrations at each location. Total experimental time was 11 minutes, during which time the data collection was briefly stopped 4 times to take DRS spectra (incoherent DRS broadband photons would otherwise interfere with DCS signals).

Location	Fiber spacing	Figure 7 location
Pedicle (artery)	1 mm	Top left, right
Flap, <i>muscle side</i>	1 mm	Bottom, right
Flap, <i>skin side</i>	1 mm, 5 mm	Bottom, left

As a proxy for relative blood flow, we primarily concerned ourselves with the correlation decay time constant. We determined this time constant by several means, including fitting to

multi-exponential decay models and quantitative moment analysis, and we report each decay time constant, when possible, as τ in units of μs .

Biological processes such as blood pressure fluctuations impart non-exponential functions atop the decay curve, complicating the fitting process. In some cases it is required therefore that alternatives be explored as exponential fitting will not converge. Alternative linear methods of fitting decay curves may hold promise for a simple and robust solution for continuous monitoring and triggering of alarms in the case of reduced perfusion in a failing flap.

3.1 Multi-exponential fitting of correlation decay constants

The decay in the intensity correlation function arising from diffusion and flow is generally given to be exponential in nature and can often be fitted with standard multi-exponential fitting algorithms (Eq. 2).

$$\sum_i a_i e^{-t/\tau_i} \quad \text{Equation 2}$$

The degree to which the data is mono- versus multi-exponential in nature is determined by the cross section of tissue and moving scatterers mediating photon transport during the multiple scattering processes. For our purposes we fit to the model which provided the lowest residuals after fitting. If there was difficulty with convergence, we switched to alternative methods in this preliminary analysis (see below). All fitting was performed in Origin 2015.

3.2 First Moment determination of correlation decay constants

In cases where data is complicated by non-exponential decays and features, multi-exponential fitting was abandoned in these initial validation trials in favor of linear methods, including determination of the centroid of the decay curve, or the first moment, M_1 :

$$M_1 = \frac{\int t f(t) dt}{\int f(t) dt} \quad \text{Equation 3}$$

Where the data are first baseline corrected subtracting 1 from each data point. It is worth noting that in Eq. 3, the contribution from longer time constants is massive, and so any deviation from the mean becomes a dominant factor, and so the moments were computed from the minimum time bin until the data had first reached an asymptote at 1 (which become 0 after requisite baseline correction).

3.3 Linear regression fitting of correlation decay constants

Standard linear regression fitting was also pursued for the noisiest, most complex, or lowest signal-level data.

3.4 Arterial blood flow analysis

Arterial blood flow was found to be complicated by non-exponential factors, precluding the application of standard fitting methods. We instead use the centroid of the intensity autocorrelation functions according to Equation 3.

3.5 Flap (muscle side) blood flow analysis

Using a single exponential fit yielded the lowest error in fit. The resulting plot closely follows the clamping time schedule and demonstrates a decrease in relative blood flow during clamping.

3.6 Skin blood flow analysis

The 2mm spacing yielded uncomplicated autocorrelation curves for multiexponential fitting. We fit to a 3 exponential model and yielded two components which were within the time constraints of the expected blood flow, while one component, τ_3 , fit to long time constant (1s) noise factors and yielded little relevant data.

A delay in the rise in τ , as compared with arterial correlation τ measurements, is observed in the trans-skin 2 mm spacing data as shown above in Figure 11. The lagging response to arterial blockage this is not unexpected, however the same lag is not seen in the muscle side data presented above. This merits further investigation to determine if it is a common relationship.

5mm spacing skin blood flow was found to be complicated by non-exponential factors, preventing standard multi-exponential fitting methods. We instead used linear fitting of the normalized autocorrelation functions, and extracted the y-intercept as a proxy for decay constant (Figure 12). We also determined the centroid of the correlation and yielded a similar plot, however this required user intervention to determine the stopping point of the centroid calculation (to eliminate dominant noise from the long time scale regions, Figure 13).

3.7 DRS data analysis

DRS data were collected at four points during the ~11 minute long clamping trial, and analysis was performed *ex post facto* by our collaborators at University of Michigan to construct a model and return O_2SAT at the skin.

A Monte Carlo lookup table-based inverse model was employed on the measured diffuse reflectance spectra to estimate a total hemoglobin concentration and oxygen saturation. The lookup table (LUT) was created using the embedded Monte Carlo codes in ZEMAX®. The source fiber (NA = 0.22, core dia. = 200 μm) and detector fiber (NA = 0.22, core dia. = 105 μm) were modeled in a non-sequential ray tracing mode in ZEMAX. A total of 252 separate simulations using 21 increments for the reduced scattering coefficient (0 ~ 40 cm^{-1}) and 12

increments for absorption coefficients (0.01, 0.5 and 1 ~ 19 cm⁻¹) were performed to create the LUT (Fig 14(a)).

The forward model generated diffuse reflectance spectra using a power law model for reduced scattering and a linear combination of oxy and deoxy- hemoglobin molar extinction for absorption. The sum of square errors was calculated between the modeled and the measured reflectance. The varying parameters were iteratively updated until the sum of squares was minimized. An interior-point non-linear optimization in MATLAB was employed for the optimization algorithm.

	Estimated parameters for each clamping status			
	Fully Clamped	Right after unclamping (within 30 sec.)	Unclamped (1 min. after unclamping)	Unclamped (10 min. after unclamping)
Total [Hb] (μM)	4.2	19.5	8.2	8.5
Oxygen Saturation (%)	38.6	92.8	63.5	65.5

4. CONCLUSIONS

In-vivo and non-invasive assessment of neovascularization within buried free maxillofacial flaps is positioned to provide early detection of flap failure and therefore to increase the salvage rate and outcomes of patients. Here, we used two optical techniques (DRS and DCS) to monitor blood flow in a porcine model for a buried free flap while blood supply was reduced via arterial clamping. Preliminary data analysis suggests that the system is highly sensitive even in direct monitoring of the microvascular perfusion within the flap. It is critical that a robust method of fitting the correlation plots is developed to produce an autocorrelation time constant with sufficient repeatability to be of clinical utility. Additional data will allow the refinement and validation of several models which provided impressive results when subjected to this dataset. These fitting tools are aimed to provide a quantitative measure of perfusion and the decrease of such prior to flap failure with as early a warning as possible.

Studies on multiple additional animal models are planned, as are 30 long-term (3 week) monitoring trials of free flaps in a porcine model.

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Figure 1.
(left) Artist's depiction of final instrument. *(right)* Depiction of implantable optical probe on pedicle (artery) feeding a buried free flap.

Figure 2. (left) Functional diagram of a typical DCS experiment. (right) Correlation functions resulting from two blood flow conditions within the finger: One during extended garroting (strangulation), resulting in slowing of blood flow [long correlation fall time], and one during the recovery phase, in which blood flow is increased [fast correlation fall time].

Figure 3.
(left) An exterior view of the delivered prototype showing fiber connections on front panel.
(right) A top interior view of the deliverable, showing control boards, spectrometer, two photon counters (Excelitas SPCM-AQRH), and 3 light sources (2 DCS lasers, one DRS LED).

Figure 4. Software GUI developed at RMD to control a DCS/DRS of up to 4 DCS and 1 DRS channels. Relative blood flow index can be tracked via a variety of correlation decay fitting methods

Figure 5.

A DCS skin probe of silicone slab type on human wrist. The probe has the option to include a Velcro strap, which is featured here

Figure 6.

Left: Implantable probe design using angle-polished fibers. Final entry angle is $\sim 60^\circ$ from normal. Aramid garrotes are potted within the grey epoxy block. **Right:** Implantable probe design using silvered RA prim potted in epoxy. Also potted within the epoxy is a collar of PTFE for securing to tissue or vein/artery. Signal levels from each device were similar, as were ad-hoc DCS evaluations on the human thumb. Photos of the devices in use are shown in the *Results and Discussion* section.

Figure 7.

Four views of the RMD perfusion monitor probes in a porcine buried free flap model. **Top, left:** Pedicle prototype implantable probe of angled-fiber type. PDMS-coated aramid garrotes secure the probe to the artery. **Top, right:** Pedicle with sample probe and a Hoffman-type screw clamp to occlude flow in a controlled manner. **Bottom, left:** Skin side of the free flap probed by a flexible PDMS skin probe incorporating multiple spacings of DCS fibers and a DRS probe at ~1.5 mm source-detector fiber spacing. **Bottom, right:** Implantable prototype probe of RA prism type sutured to the free flap, muscle side. Sutures are holding PDMS coated PTFE wings, which are alternatively able to wrap an artery or vein on the pedicle.

Figure 8.
Left: Pseudo-quantitative clamping graph based upon observation of surgeon controlling the Hoffman screw clamp, for use as an overlay to DCS data. *Right:* Observations of surgeon in table form on blood flow and clamping upon which overlay is based.

Figure 9. Correlation fall time as measured by the centroid (first moment) method of arterial blood flow. **Overlay, green:** Pseudo-quantitative clamping graph based upon observation of surgeon.

Figure 10. Correlation fall time as measured by single exponential fit of microcapillary blood flow in the muscle side of a model for a buried free flap. **Overlay, green:** Pseudo-quantitative clamping graph based upon observation of surgeon

Figure 11.

Correlation fall time as measured by a 3 exponential fit (showing 2 components) of microcapillary blood flow in the skin side, spacing (depth) 2mm, of a porcine model for a buried free flap. **Overlay, green:** Pseudo-quantitative clamping graph based upon observation of surgeon

Figure 12.

Correlation fall time as measured by the y-intercept of linear fits to the normalized intensity autocorrelation functions arising from microcapillary blood flow in the skin side of the free flap, spacing (depth) 5 mm, of a porcine model for a buried free flap. **Overlay, green:** Pseudo-quantitative clamping graph based upon observation of surgeon

Figure 13.

Correlation fall time constant as measured by a centroid determination of the intensity autocorrelation function of the microcapillary blood flow on the skin side, spacing (depth) 5mm, of a porcine model for a buried free flap. Stopping point for moment analysis was 1 ms. **Overlay, green:** Pseudo-quantitative clamping graph based upon observation of surgeon.

Figure 14.

(a) The 2D-lookup table $[R(\mu'_s, \mu_a)]$ was created using 252 separate MC simulations. For given μ'_s , and μ_a , reflectance was calculated by each MC simulation (b) Representative inverse MCLUT model (red dot) fit for the measured reflectance spectrum (solid black).