PROSPECTIVE ANALYSIS OF FLAP PERFUSION BY MEASURING CAPILLARY GLUCOSE LEVELS IN PEDICLED FLAP AND FREE TISSUE TRANSFER

A dissertation submitted to the Tamil Nadu Dr M.G.R. Medical university in partial fulfillment of the requirement of the award of M.Ch. Branch III (Plastic surgery) Degree August 2011-2013

CERTIFICATE

This is to certify that the dissertation entitled "**Prospective analysis of flap perfusion by measuring Capillary Glucose levels in pedicled flap and free tissue transfe**r" is a bonafide work done by **Dr. Mukesh Kumar Sharma**, CMC Vellore.In partial fulfilment of the University rules and regulations for award of M.Ch in Plastic Surgery under my guidance and supervision during the academic year 2011- 2014.

Guide:

Dr Kingsly Paul M
Professor
Department of Plastic Surgery
Christian Medical College
Vellore

Co Guide:

Dr Elvino Barreto
Associate Professor
Department of Plastic Surgery
Christian Medical College
Vellore

Head of Department:

Dr. Ashish Kumar Gupta
Professor and Head
Christian Medical College
Vellore

Principal

Christian Medical College
Vellore

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Page count:	72
Word count:	11,089
Character count:	62,126
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Introduction

Flap surgery is one of the most commonly performed surgeries in the department of plastic surgery. A valid and reliable flap monitoring tool is required for early detection of flap ischemia so that timely measures can be taken for the salvage of failing flap.

Early detection of circulatory compromise allows timely intervention for salvage of a failing flap before irreversible damage occurs. The window period between onset of circulatory compromise and salvage surgery is crucial for the outcome of flap surgery.((1)(2)(3)

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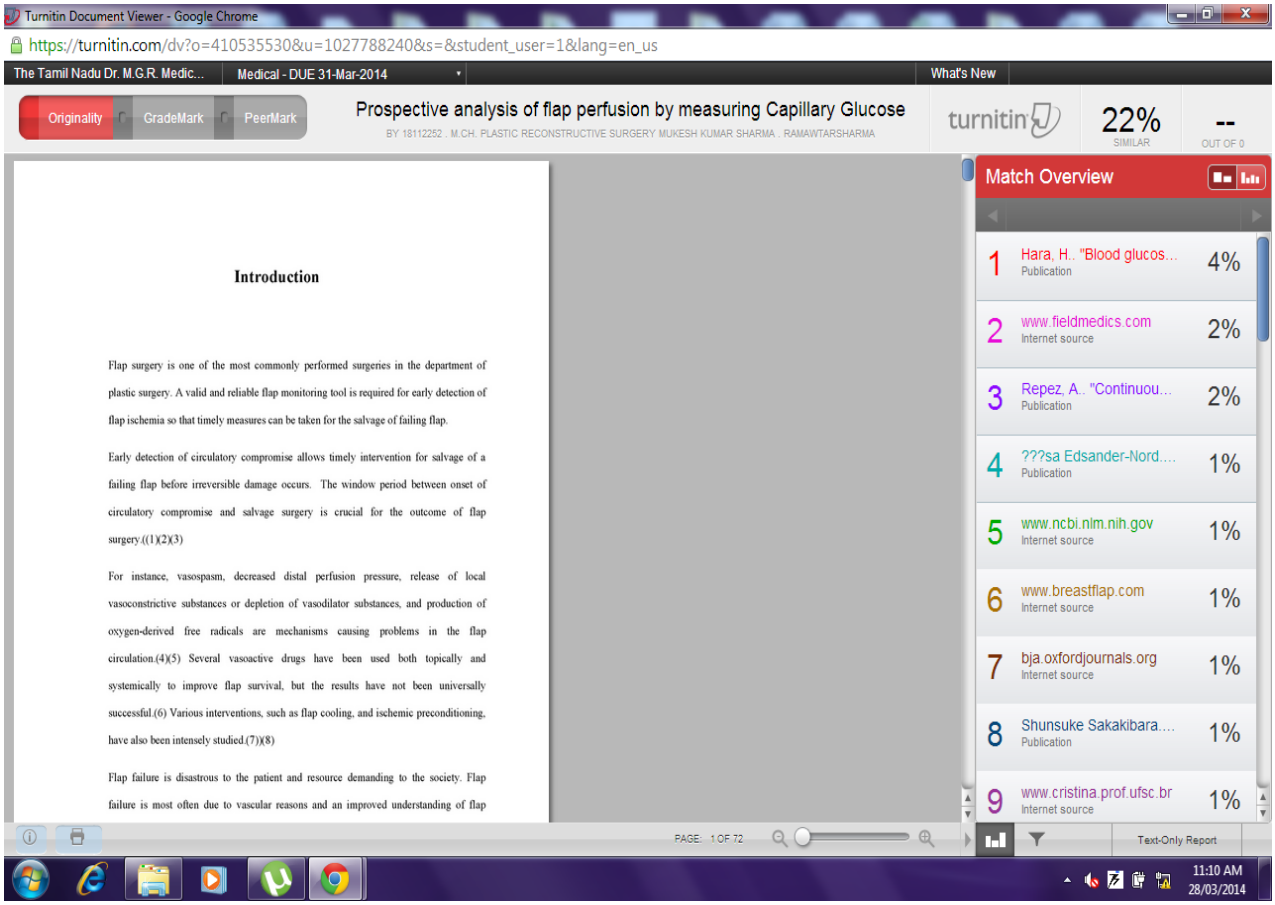
Flap failure is disastrous to the patient and resource demanding to the society. Flap failure is most often due to vascular reasons and an improved understanding of flap hemodynamics and how it responds to ischemia are thus of central importance for attempts to minimize morbidity.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Senior PG Student
Department of Plastic Surgery
Christian Medical College
Vellore 632 004

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Prospective analysis offlap perfusion bymeasuringCapillary Glucose levels in pedicled flap and free tissue transfer.
Dr. Mukesh Kumar Sharma, Senior PG registrar, Emp. No. 20818, Dr. Kingsly Paul M, Professor, Emp. No. 30650, Dr. Elvino Barreto, Emp. No.32679, Plastic Surgery.

Ref: IRB Min No: 8203 dated 13.02.2013

Dear Dr. Mukesh Kumar Sharma,

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Nihal Thomas, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. Nihal Thomas
Secretary (Ethics Committee)
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Dear Dr. Mukesh Kumar Sharma,

The Institutional Review Board (Blue, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project entitled "Prospective analysis offlap perfusion bymeasuring Capillary Glucose levels in pedicled flap and free tissue transfer." on February 13, 2013.

The Committees reviewed the following documents:

1. Format for application to IRB submission
2. Patient Information Sheet and Informed Consent Form (English, Tamil, Hindi and Bengali)
3. Proforma
4. Cvs of Drs. Mukesh Kumar Sharma, Kingsly Paul.
5. A CD containing documents 1 - 4

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The following Institutional Review Board (Research & Ethics Committee) members were present at the meeting held on February 13, 2013 in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore 632002.

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Dr. Benjamin Perakath	MBBS, MS, FRCS	Professor, Surgery (Colorectal), CMC.	Internal, Clinician
Dr. Ranjith K Moorthy	MBBS MCh	Professor, Neurological Sciences, CMC	Internal, Clinician
Dr. P. Prasanna Samuel	B.Sc, M.Sc, PhD	Professor Dept. of Biostatistics, CMC	Internal, Statistician
Dr. Balamugesh	MBBS, MD(Int Med), DM, FCCP (USA)	Professor, Dept. of Pulmonary Medicine, CMC.	Internal, Clinician
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Additional Vice Principal (Research)

Dr. Nihal Thomas	MD MNAMS DNB(Endo) FRACP(Endo) FRCP(Edin)	Secretary IRB (EC)& Dy. Chairperson (IRB), Professor of Endocrinology & Addl. Vice Principal (Research), CMC.	Internal, Clinician

We approve the project to be conducted as presented.

The Institutional Ethics Committee expects to be informed about the progress of the project, any serious adverse events occurring in the course of the project, any changes in the protocol and the patient information/informed consent. And on completion of the study you are expected to submit a copy of the final report.

A sum of Rs. 39,100/- (Rupees Thirty Nine Thousand One Hundred only) will be granted for 1 year.

Yours sincerely

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

Dr Nihal Thomas
MBBS MD MNAMS DNB (Endo) FRACP(Endo) FRCP(Edin)
Secretary (Ethics Committee)
Institutional Review Board

CC: Dr. Kingsly Paul, Department of Plastic Surgery

ACKNOWLEDGEMENT

I wish to express my deepest sense of gratitude to my teacher Prof. Kingsly Paul who has played an active role in this work and also was a constant source of inspiration and encouragement to me throughout.

I sincerely thank The Director and the members of the IRB committee, Christian Medical College, Vellore for approving my thesis topic and giving me permission to conduct the study.

I owe my sincere thanks to my teachers, Prof. Ashish Kumar Gupta, Dr. Elvino Barreto and Dr Shashank Lamba who gave valuable advice, support and encouragement throughout my work.

I sincerely acknowledge the help of Dr Jayseelan and Miss. Tunny Sebastian Department of Biostatics in performing the statistical analysis of data Dept CEU. I am thankful to Ms. Shabana for helping me in formatting of disseratation.

I am also grateful to Sister Kalaivani and the sisters of Q1 WEST ward for all their support.

I am also grateful to other faculty members and all my post-graduate colleagues for their practical suggestions and help rendered in the preparation of this work.

I also acknowledge the constant support of my wife Neha and my family throughout the course of my education. Last but not the least I thank all the patients without whom this study would not have been possible.

INDEX

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To minimize the incidence of flap failure early detection of postoperative flap ischemia is necessary for timely re-exploration.(9) However, various monitoring techniques in the literature have not fulfilled all requirements to be universally applicable for this purpose .(10) (11) (12)(13) (14) (15)(16)(17)(18)

The ideal monitoring method would be non-invasive, reliable, continuous, accurate, and easy to use even for the inexperienced personnel, inexpensive, and provide real-time information. Although a multitude of monitoring methods has been introduced, clinical observation is still the gold standard of flap assessment, despite its inherent problems.(19)(20)

The present study is to evaluate flap capillary glucose level measurement as a monitoring method to evaluate flap viability.

Aims and Objectives

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To assess the efficacy of capillary glucose level and its diagnostic validity in the post-operative monitoring of pedicled flap and free tissue transfer.

Review of Literature

Review of Literature

Functional anatomy of circulation

The heart constantly pumps blood throughout the body through two anatomically separate vascular pumps. The pulmonary circulation conveys deoxygenated blood from the right ventricle to the lungs via pulmonary arteries, arterioles and capillary network. The blood is oxygenated in the capillary network around the alveoli of the lungs and then progresses to the left side of the heart via the pulmonary venules and veins to the left atrium. The systemic circulation delivers this oxygenated blood from the left ventricle though out the body through arteries, arterioles and capillaries and returns it through venules, veins and finally through the inferior and superior vena cavae to the right side of the heart (Figure 1)

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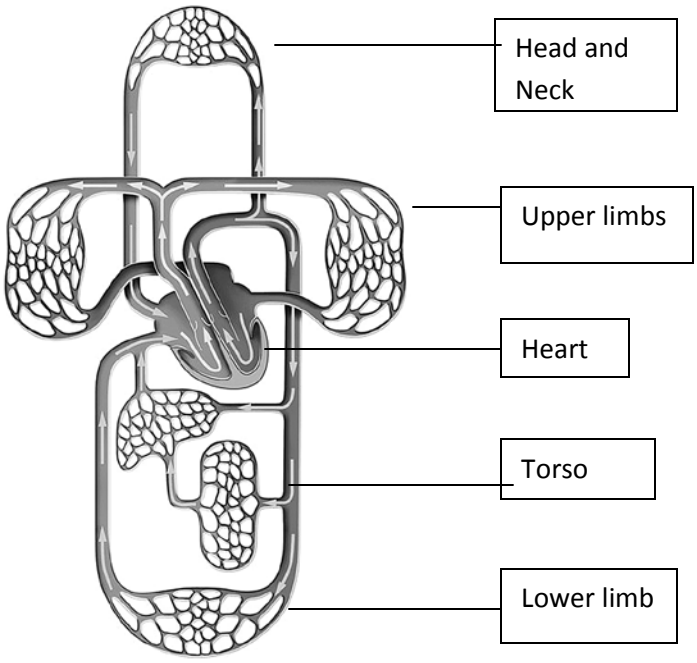


Figure1. A schematic illustration of the human circulation

Although the blood vessels in each flap tissue have their own specific characteristics, some general principles of vascular function apply to all parts of the circulation of the body. The arteries are thick walled and transport blood to the target tissues. The end branches of the arterial system, the arterioles are connected to the capillary beds. Arterioles have muscular walls that can close the vessels completely or dilate them several fold. Thus, arterioles can alter blood flow to the capillary network in response to the needs of the tissue in an efficient way. Capillaries are thin walled and allow exchange of electrolytes, nutrients, and hormones between the blood and the interstitial fluid.

Cutaneous perfusion

William Harvey first described the blood flow to the skin in 17th century .(21) Tomsa described the subdermal and dermal plexuses of the skin in 1873, and Spateholz the direct and indirect perforators to the skin In 1889.(22) Manchot detailed the cutaneous blood supply and identified distinct areas of the skin which were separately perfused by source vessel. (22) His work formed the basis of the studies of Salmon, who found that in reconstructive surgery a flap must include an arterial pedicle.(22) The vasculature of the skin and subcutis is believed to consist of five vascular plexuses (Figure 2). The most superficial is the subepidermal plexus, beneath which run the dermal, subdermal, subcutaneous, and the fascial plexuses. Each plexus consists of a horizontal, fine meshwork of interconnecting vessels. The plexuses have a huge capacity for distributing blood flow to the skin and subcutis. The dermal plexus has muscular arteriolar vessels and is the main thermoregulatory system, while the subdermal plexus has thin-walled capillaries and is the main site for nutrient exchange. The blood flow to the vascular plexuses of the skin and subcutis is supplied through the perforator arteries, which arise from source arteries below the deep cutaneous fascia.(23)

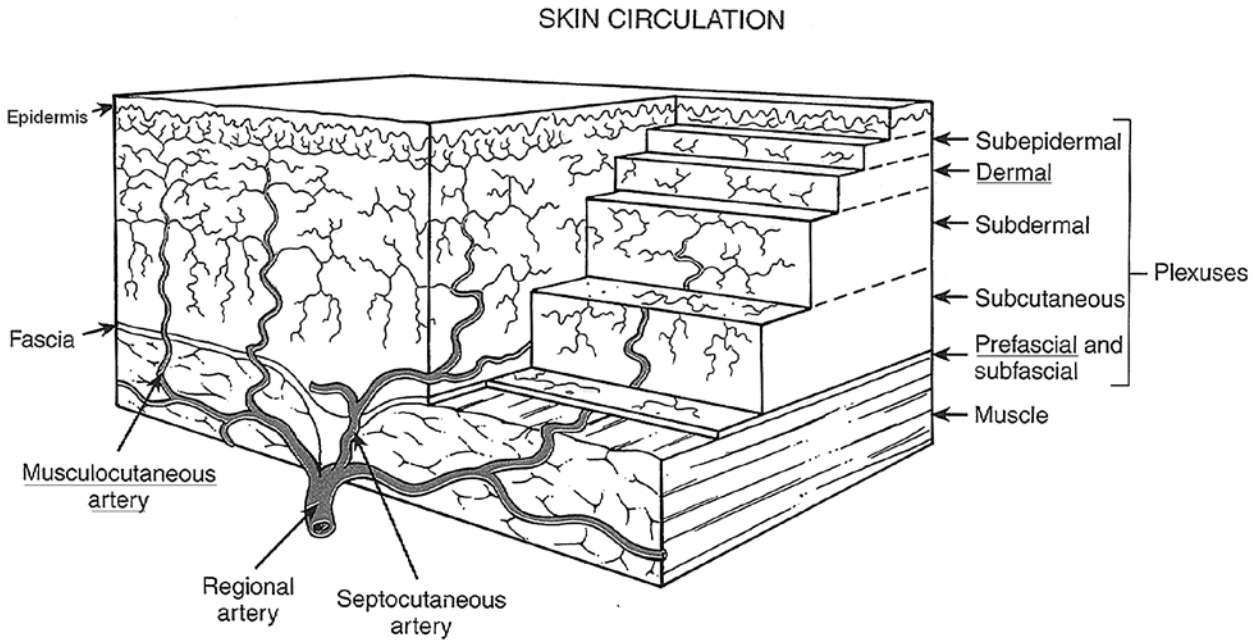


Figure 2.A schematic representation of the vascular structure of the skin and subcutis. (Mathes and Nahai 1997).

Physiology of circulation regulating blood flow in flaps

In healthy adults with a body weight of 70 kg the cardiac output is approximately 5 liters per min. (24) The blood flow defined as the amount of blood streaming through a certain point in the circulation in a given period of time. Blood flow is calculated by Darcy's law.

$$\mathbf{BF = \Delta P/R} \qquad \text{(equation 1)}$$

BF -blood flow (L/min),

ΔP -pressure difference between the two measuring points of the vessel (mmHg),

R - is the vascular resistance.(mmHg/L/min).(25)(26)(24)

Vascular resistance is thus inversely related to blood flow, and is an important regulator of the blood flow in a flap.(26) The diameter of the vessel is very important for its ability to conduct blood. The blood flow in periphery of the vessel is quite slow, whereas its more rapid in the middle of the vessel (laminar flow). Thus, in a vessel with a small diameter, almost all the blood is close to the wall, and the proportion of blood flowing rapidly is small.

The blood flow rate is determined by Poiseuille's law.

$$\mathbf{BF = \pi \Delta P r4/8\eta L} \qquad \text{(equation 2)}$$

BF = Rate of blood flow (ml/min)

ΔP = Pressure difference between the measuring points of the vessel (mmHg)

R = Radius of the vessel (m)

L = Length of the vessel (m)

η = Viscosity of the blood (kg/s/m),

π = 3.1416

Therefore, in addition to vascular resistance the diameters of blood vessels substantially regulate perfusion of the flap.

Blood viscosity is an important variable in Poiseuille's law. If all other factors stay constant, the higher the viscosity of the blood, the lower the flow is in a vessel. The viscosity of blood of healthy persons (with a hematocrit 40) is about three times greater than that of water. The high

number of suspended red cells is the main determinant of blood viscosity.(24) Nitric oxide mediated vasodilation may also contribute to perfusion.(27)

Perfusion increases immediately after skeletal muscle denervation, which causes arteriolar vasodilatation and increased capillary perfusion.(28)(29)(30) It is known that the perfusion of free flaps increases two weeks to three months postoperatively, as assessed by Doppler ultrasound measurements.(31) Denervation of a cutaneous flap decreases its vascular resistance. (32)(25) Experimentally it has been shown that blood flow increases in skin island flaps after sympathectomy, which is most likely due to vasodilation caused by a lack of sympathetic neural regulation in arterioles.(33) Walkinshaw showed that the recovery of perfusion after artery and vein anastomosis in a free rat groin flap was not affected by changes in the external vascular diameter of the pedicle which indicates that diameter of pedicle vessels may not be the only factor determining the perfusion.(4).

Blood pressure (BP) is defined as the force exerted by circulating blood on the walls of blood vessels. As blood flows through the arteries, arterioles, capillaries, and veins the blood pressure gradually decreases**.** For each heartbeat, the blood pressure varies between systolic and diastolic blood pressure. The mean arterial is the average arterial pressure (mmHg) during a single cardiac cycle.

$$MAP = (CO \times SVR) + CVP \qquad \text{(equation 3)}$$

OR

$$MAPa = DP + 1/3\ (SP-DP) \qquad \text{(equation 4)}$$

CO = Cardiac output (L/min),

SVR = Systemic vascular resistance (mmHg/L/min)

CVP = Central venous pressure (mmHg).

MAP defines the perfusion pressure of the tissues in the body. Mean arterial pressure more than 60 mmHg, is required to maintain the perfusion of the organs in a normal living individual under most conditions**.** If the MAP falls significantly below 60 mmHg for any appreciable amount of time, the end organ will become ischemic.

The terms blood flow and perfusion are often used as synonyms, although they are not quite the same. The term flap blood perfusion (BFPET) is used to describe flap tissue perfusion (ml blood / min / volume of tissue).

Local control of blood flow in flaps

Changes in perfusion pressure elicit changes in vascular resistance is an attempt of the tissue to maintain a constant level of oxygen delivery. These changes are elicited to allow constant blood flow and are called autoregulation, which is the ability of each tissue to control its blood flow according to its metabolic needs. Autoregulation is one of the fundamental principles of circulatory function. (34)

Metabolically active tissues (e.g. active muscles) need much more blood than muscles at rest. Arterial blood pressure is a determinant of the number of capillaries with red blood cell transit. It is decreased if artery supplying to the tissue is occluded or vasoconstricted by an oversupply of oxygen.(35) However, under regular conditions it is not possible for heart to increase its output by more than five- to seven-fold and to increase the blood flow everywhere in the body when a particular tissue is in need of more blood flow. In an intact living organ, specific local vascular

effects are provided by the neural control of the circulation to regulate tissue perfusion. Moreover, the microvessels of each organ continuously monitor the tissue needs for oxygen and other nutrients, as well as the accumulation of tissue waste products such as carbon dioxide. Although sympathetic innervations regulating vascular responsiveness of tissues is reduced by flap elevation, local and circulating factors still persist that control vascular responses. (36)(37)(38)(39)(24)

Vascular smooth muscle can be stimulated to contract by multiple types of signals: e.g. neural signals, muscle stretching, and hormonal stimulation. Experimentally it has been found that proximal sympathectomy of a muscle flap with somatic denervation leads to increased capillary perfusion and hyperreactivity to vasoactive substances.(39) Another experimental work with rats showed that microcirculatory blood flow responds to catecholamine in denervated tissue and that ischemia aggravates vasospasm that has been induced by intra-arterial norepinephrine.(40) In vitro papaverine elicits a concentration-dependent relaxation of rabbit carotid artery rings precontracted with norepinephrine.(41)

A totally isolated artery preparation contracts when norepinephrine is added, and relaxed by acetylcholine. Endothelial cells are apparently needed for the relaxation.(42) Intraluminal papaverine increases the lumen size of the isolated human internal mammary artery (IMA).(43) The endothelium is a single layer of cells of the innermost vascular wall. It is a source of vasoactive substances (prostacyclin, NO, endothelium-derived hyperpolarizing factor and contracting factor endothelin) that can cause contraction or relaxation of vascular smooth muscle, i.e., endothelium-mediated control of flow. According to the study by Holtz the changes in vessel diameter that follow changes in blood flow are endothelium-dependent.(44) On the other hand, Hillier concluded that the use of vasoactive agents like acetylcholine or bradykinin elicits vascular smooth muscle relaxation only in the presence of an intact endothelium.(43)

Other vasodilators, such as sodium nitroprusside or glyceryl trinitrate, are not endothelium-dependent, but cause relaxation by acting directly on the smooth muscle cells.(43)(45) Endothelial cells secrete endothelins. In the healthy human body, endothelin-1 is a vasodilator at low doses but a vasoconstrictor causing strong and long-lasting vasoconstriction at large doses.(46)(47) EDRF is a vasodilating substance. In addition to the relaxation of the arterial wall, EDRF also increases the dimensions of the upstream large arterial vessels.(42) This dilation appears to be an effect of vasodilator substances that diffuse into the precapillary sphincters, metarterioles, and arterioles. The state of tissue nutrition is more or less proportional to the number of precapillary sphincters that are open at any specific moment. The precapillary sphincters open and close cyclically many times in a minute, and the duration of the open phase depends on the metabolic needs of the tissues. This phenomenon is named vasomotion.(24)

The vasodilating substances appear to be released from the tissue mainly by hypoxia. Decreased availability of oxygen leads to release of adenosine and lactic acid in the tissue. During muscle ischemia, tissue levels of ATP decrease substantially.(48) Exogenous adenosine appears to protect against ischemia-reperfusion injury as it is a vasodilator.(49) Adenosine also causes inhibition of neutrophil-mediated cellular injury due to prolonged ischemia by inhibiting neutrophil-mediated free radical production.(50)(49) Adenosine is a protective factor in the setting of ischemia-reperfusion injury by limitng release of inflammatory mediators and by activating intracellular antioxidant systems.(51) Adenosine is of proven Clinical efficacy in pretreatment of limb transplantation or microvascular tissue transfer by providing protection against ischemia-reperfusion injury.(6)

The local blood flow regulation in a flap is explained by two basic theories, when either tissue metabolism or oxygen supplies changes:

1) Metabolic theory postulates that reduced arterial inflow causes a decreased rate of washout of aerobic vasodilator metabolites, such as CO2, ATP, histamine, glucose, potassium and hydrogen ions. Reduced arterial inflow reduces further the tissue O2 pressure and this causes typically subsequent vasodilation.

2) The myogenic mechanism theory postulates that the arterioles or resistance vessels respond by vasoconstriction to a stimulus of intravascular pressure elevation and that this increases tension and stretching of smooth muscle cells.(34) Both theories explain local blood flow regulation of a free flap in relation to the metabolic needs of the tissues and a combination of these two mechanisms is probably the most accurate explanation of local blood flow regulation.(52)

Perfusion heterogeneity in flaps

Perfusion heterogeneity is defined as the degree of uneven blood flow among blood vessels or different tissues. The exchange of small particles such as oxygen in capillaries is largely dependent on perfusion, which may be distributed spatially uniformly or not (53) The efficacy of tissue oxygenation and oxygen delivery to the flaps is greatly influenced by this spatial flow heterogeneity.(54) Moreover, there is great variation of perfusion also over time. The physiological significance of this phenomenon called temporal heterogeneity is unclear. The unipedicled TRAM flap or breast reconstruction was first described by Scheflan and Dinner**.** The flap was divided into four equal parts. The zones of perfusion were numbered based on the idea that perfusion zones immediately adjacent to the territory of the vascular pedicle have better perfusion than zones farther away**.** (Figure3B). These perfusion zones became better known after the publication by Hartrampf (55) (Figure 3A).

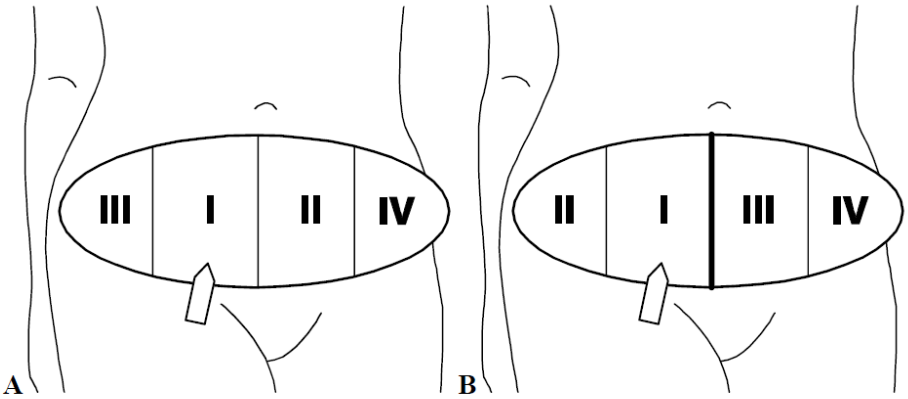


Figure3. A Conventional perfusion zones of TRAM flap (Hartrampf et al. 1982). **B** Zones of lower abdominal flap suggested by Holm (Holm et al. 2006). I = zone I presenting the region of the abdominal flap closest to the vascular pedicle of the flap; II = zone II; III = zone III; IV = zone IV, which is usually discarded from the abdominal flap in reconstructions.

Oxygen transport of flap

Oxygen is transported from the inhaled air to each cell and extracellular matrix in the body. Transport follows the principle that gases move from an area of higher concentration to areas of lower concentration.

At sea level the atmospheric pressure is 760 mmHg**.** Air consists of 21 % oxygen, 78 % nitrogen and rest is CO2, argon and helium**.** The inspired air is warmed and humidified by the upper respiratory tract before it reaches the trachea**.** The *p*O2 in the trachea is 150 mmHg**.** By the time oxygen reaches the alveoli the *p*O2 has fallen to about 100 mmHg. This is because the *p*O2 of the gas in the alveoli (*pa*O2) is a balance between the removal of oxygen by the pulmonary capillaries and its continuous supply by alveolar ventilation.(24)

Deoxygenated blood (low *p*O2 -40 mmHg) is collected from tissues and returned to heart via major veins**.** Then it goes to the lungs via the pulmonary arteries**.** The pulmonary arteries forms a

capillary network around alveoli. Oxygen is transported from alveoli (100 mmHg) to pulmonary capillaries (40 mmHg). Oxygenated blood moves to left side of heart (via pulmonary veins) and pumped to the systemic tissues**.).** Ventilation / perfusion mismatch, shunting, and slow diffusion may cause the *p*O2 in the pulmonary veins to be less than the *pa*O2.(Guyton and Hall 2006**)**

Oxygen is transported in blood mostly bound to hemoglobin, and in a minor degree as dissolved form in plasma**.** At normal *p*O2 only 3 mL of oxygen will be dissolved in a liter of plasma. Each gram of fully saturated hemoglobin can carry 1.34 mL of oxygen**.** Therefore, every liter of blood with a Hb concentration of 150 g/L can carry about 200 mL of oxygen, if the hemoglobin is 100 % saturated. (24)

By increasing *p*O2(Breathing 100 % O2) of oxygen in arterial blood a small amount of extra oxygen will dissolve in the plasma (at a rate of 0.003 ml O2 / 100mL of blood / mmHg *p*O2) but there will be no significant increase in the amount carried by hemoglobin as it is already >95 % saturated with oxygen. Oxygen delivery to the tissues depends on three factors: hemoglobin concentration, cardiac output and oxygenation**.**(24) The *p*O2 reaches its nadir (4-20 mmHg) in the mitochondria.(56) This decrease in *p*O2 from air to mitochondria is known as the oxygen cascade**.** The quantity of oxygen made available to the body is known as the oxygen delivery. Oxygen delivery is directly proportional to the cardiac output and the arterial oxygen content, i.e., 5,000 ml blood / min x 200 ml O2 / 1,000 ml blood = 1,000mL O2 / min.

$$DO2 = CO \times HbC \times 1.34 \times SaO2 \qquad \text{(equation 5)}$$

DO2 = Oxygen delivery (ml/min)

CO = Cardiac output in liters per minute

HbC = Concentration of hemoglobin in grams per a liter of blood

1.34 is the amount of oxygen in milliliters per fully saturated hemoglobin gram

SaO2 = percentage of hemoglobin O2 saturation.

Any reduction in cardiac output, hemoglobin concentration, or hemoglobin saturation of 02 will result in an inadequate delivery of oxygen**.** If oxygen delivery falls relative to oxygen consumption, the tissues try to extract more oxygen from the hemoglobin. A reduction in the saturation of mixed venous blood below 70 % cannot be compensated for by increased oxygen extraction, and thus results in anaerobic metabolism and lactic acidosis.(24)

Clinical methods to assess flap blood flow

Accurate assessment of flap perfusion is a challenge to the surgeon and nursing staff**.** A plenitude of techniques for monitoring flap blood flow has been developed. To minimize flap failure due to circulatory impairment, a reliable diagnostic method that gives early warning signals is needed**.** Although a multitude of methods to assess flap blood flow are available, there is still no single method widely accepted for clinical use**.**

Ideal monitoring method is defined by criteria given by Creez and Miller in 1975.(57)

It should be

1) Simple and Harmless

2) Objective

3) Reliable

4) Continuous

5) Accurate

6) Inexpensive

7) Provide real-time information

8) Easy to use even for the inexperienced personnel.[1]

According to Jones, the ideal monitoring method should be noninvasive, reliable, objectively repeatable, promptly reactive to perfusion changes, appropriate for continuous monitoring in all kinds of free tissue transfers, usable also by unskilled, and not too expensive**.**(58) In addition to conventional clinical monitoring, various methods of monitoring have been developed and used. Photopletysmography, laser Doppler, and ultrasonic Doppler, microdialysis, near-infrared spectroscopy, dynamic CT, and MRI, have all been used. None of these methods has become a gold standard.(59)(60)(61)(62)(63)(64)(65)

Most surgical complications vascular insufficiency usually occurs within 3 days of surgery. However, late thrombosis can occur and is often associated with a local infection or mechanical compression of the vascular pedicle. Therefore routine monitoring of all flaps is key for salvage.(66)

Monitoring by clinical means are often unreliable and observer dependent. Tissue color, turgor, temperature, capillary refill, and bleeding time are subjective variables that may be dependent on room-light, temperature, and the experience of the observer**.** Many monitoring methods are based on relative measuring results and cannot be directly compared inter-individually**.** The intricacies of flap microcirculation are frequently difficult to assess despite all examination techniques available today. External Doppler probe, endoscopy, monitoring island flap, or even leaving the wound temporarily open, might be used to monitor buried flaps.

Quantitative measurements of BF have been made with various radioactive tracers and dyes**.**

Two distinguished classes of method are

a) Total organ blood flow measurement

b) Measurement of organ perfusion (i.e. blood flow per unit mass/ volume).

1) Tissue oxygen tension (*p*tiO2) measurement

Local partial pressure of oxygen in a specific tissue is measured in terms of Tissue oxygen tension (*p*tiO2 e.g. flap tissue. It may be thought of as the local expression of global DO2 (equation 5) in a particular tissue**.** At a given time, Tissue oxygen tension defines the balance between oxygen perfusion and consumption in the organ or tissue**.** Tissue oxygen tension may be measured in any tissue but values in peripheral subcutaneous tissue are the most widely reported.(67)

The effect of absolute pressure on blood oxygenation is determined by Henry's law, which states that the volume of a gas dissolved in a liquid is proportional to its partial pressure.

$$C = K\,Px \qquad \text{(equation 6)}$$

C = Concentration of gas dissolved in the liquid (mol/L)

K = Solubility constant (mol/L atm)

Px = Partial pressure of the gas on the liquid (atm)

Tissue oxygen tension can be measured by a probe that consists of a silver anode and a platinum cathode. The resulting electrical current is directly proportional to the number of oxygen molecules reduced at the cathode. Since Hunt (68) described a new method of determining tissue oxygen tension, several clinical applications using this method have been introduced(69)(70)(71)(14)

Previously, transcutaneous oxygen tension (*p*tcO2) was used experimentally and clinically for determining the microcirculation of cutaneous tissue.(72)(73) Tuominen found that laser Doppler

flowmetry is a more sensitive technique than transcutaneous flap oxygen tension to monitor hemodynamic changes during TRAM flap operation.(74)

The oxygen diffuses from the tissue through the catheter tube into its inner electrolyte chamber. In this chamber, O2 is transformed to hydroxyl (OH-) ions at a negatively polarized noble metal electrode, the polarographic cathode. The anode of the circuit is at a distance of approximately 30 mm from the rear of the electrolyte chamber. The current from the O2 reduction is the raw signal of the sensor. The proximal end of the probe is closed by an electrical cable connection, which is attached to a digital, bedside monitor displaying real-time *p*tiO2 values every 20 seconds.

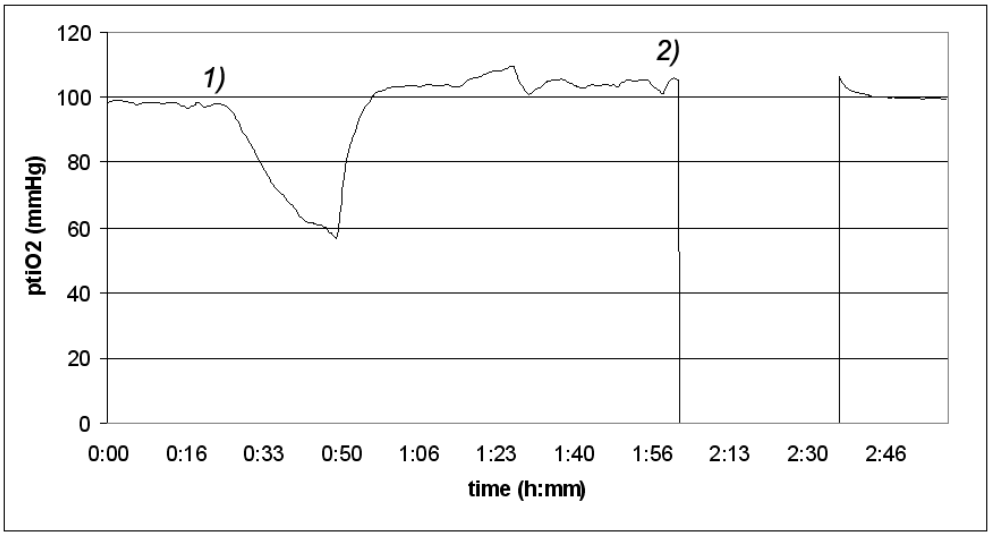


Figure 6. Sample of *p*tiO2 measurement of a free HN reconstruction flap.

The polarographic method was first introduced in the 1960s.(68) In the early 1990s, a commercially available method of polarographic measurement of tissue oxygenation was presented.(75) Since then, many studies on human tumor oxygenation have been done. This technique has been regarded as the gold standard for the measurement of hypoxia.(76)

Disadvantages of the technique include the fact that necrosis cannot be differentiated\ from viable cells, nor can acute and chronic hypoxia be separated. The use of probes is limited to superficial tissues that can be reached with the probe(20)(14)(77)

2) Doppler ultrasound

A non-invasive, real-time technique applied for many clinical purposes to provide information on blood circulation.(78) It is possible to evaluate the velocity and direction of blood flow by recording the reflected ultrasound waves (78)(79)(80) not only in large vessels but also in small ones with a diameter of less than 2 mm.(81) This technique can also be used to investigate vessel patency,(78) to evaluate vascular resistance,(82) location of the recipient artery and vein,(81)(80) and to measure blood flow velocities after surgery.(79)(80) However, the measurements can be performed only in relatively superficial regions, within reach of the ultrasound probe on the skin, and quantitative measurements are not available. The results reflect mainly blood flow in larger vessels and not in the microvasculature, since flow volume and velocity in capillaries are too low to be detected.(83)(84) However, new measurement techniques can discern somewhat lower velocities, as well.(85) Conventional Doppler imagining is based on the estimation of the mean Doppler frequency shift. Power Doppler imagining is a method based on estimating the integrated Doppler power spectrum.(86) The biggest drawbacks of this method include the inability to measure regional perfusion, the requirement of an experienced operator, and the availability of costly ultrasound device. Moreover, Doppler ultrasound can only measure velocity of moving particles in the blood stream, e.g. moving red blood cells.

3) Microdialysis

In microdialysis, a probe with a semi-permeable membrane is inserted into the tissue and transport of molecules across the membrane is measured.(87) The microdialysis probe mimics the function of a blood capillary (Figure 7).

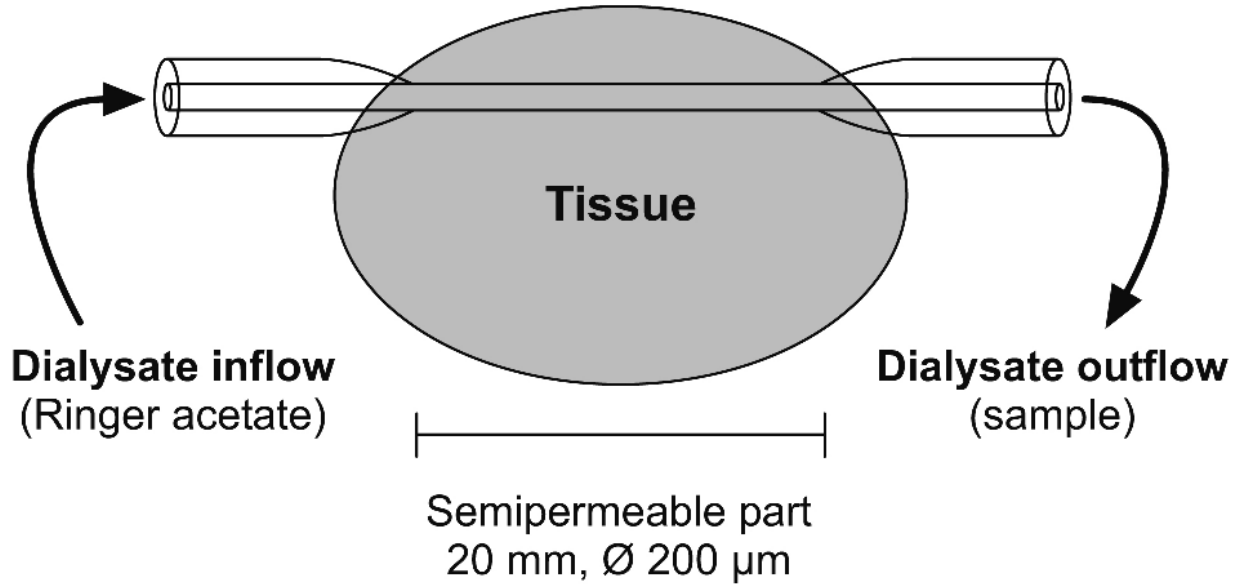


Figure 7. Schematic illustration of a microdialysis catheter inserted through tissue.

The microdialysis catheter consists of a dialysis tube that is glued to the end of a double-lumen catheter. The inlet tube of the catheter is connected to a battery-powered microinfusion pump (e.g. CMA 106 Microdialysis Pump, Figure 8B), and continuously perfused with a sterile isotonic Ringer solution at a flow rate of 0.3 microliters per minute. The solution flows in the outer cannula inside the dialysis membrane to the distal end of the catheter (Figure 7). At the tip of the microdialysis catheter there is a permeable membrane where equilibration with extracellular substances, such as glucose, takes place. The equilibrated solution (the dialysate)

flows in a retrograde direction and leaves the catheter through the inner cannula, and aliquots are collected in microvials. The vials are placed in a microdialysis analyzer, where the dialysate is analyzed bedside. The results can be viewed as a graph on a computer screen, and metabolic trends can be viewed**.**(88)(89)

Earlier microdialysis studies (90) have shown that glucose, lactate, and glycerol concentrations changes during ischemia and results were verified by Edsander-Nord.(64) decreasing glucose and pyruvate concentrations and increasing lactate and glycerol concentrations is suggestive of ischemia and thus the lactate to pyruvate ratio increases during ischemia.(64)(91) Nowak monitored tissue metabolism in the transplanted liver using microdialysis.(92)

Microdialysis is reportedly a clinically feasible and sensitive monitoring method for all kinds of microvascular flaps, especially for those in which clinical observation is difficult or impossible e.g. buried flaps.(91)(93)

4) Laser Doppler flowmetry (LDF)

Change of the frequency of light reflected from moving objects within the microcirculation of flap is converted to an electrical signal that provides a light-emitting diode display proportional to tissue blood volume and velocity, from which blood flow is calculated.(94) The sampling volume of each probe is small (~ 0.l mm3) and thus the measurements mainly reflect microcirculatory flow, but variations in perfusion over time can be measured. However, absolute measures of perfusion are not possible.(95)(96)(62)

The frequency shift of the light scattered back from moving red blood cells (Doppler effect) is given by equation 7:

$$\Delta f = vfo/c \qquad \text{(equation 7)}$$

Δf = magnitude of the frequency shift (1/s)

v = Velocity of the source with respect to the observer (m/s)

c = Velocity of the carrier wave (m/s),

fo = Unshifted frequency (1/s).

Static objects do not cause such change. The shifted backscattered light is collected by the photodetectors where it is processed and amplified. In capillary blood flow applications the Doppler shift of laser light is relatively small which is difficult to measure directly. Consequently the frequency shifted light is combined with non-shifted light to extract the information of interest.(97)

The measuring depth depends on tissue properties, e.g., wavelength of the laser light ultilized, the density and the structure of the capillary beds, and the distance between the fibers in the probe. In well-perfused organs, such as the kidney and the liver, the measuring depth of LDF is less than one millimeter, while in the intestine the measuring depth can be several millimeters. The longer the wavelength, the deeper the penetration is into the tissue. If the blood supply to a measured region is occluded, the measuring depth will increase, since the lack of blood permits more passage of light. Jones and Mayou first reported the use of LDF for monitoring free flaps in patients.(98) They found that increased postoperative blood flow indicated satisfactory free flap survival, while a reduction in flow is a warning signal of thrombosis formation. Since this preliminary report, LDF has become a widely used monitoring technique of free flaps (74)(13) Although LDF is generally considered to be a good monitoring technique of free flaps, there is also scepticism about the reliability of LDF related to motion, vibration, and location of the probe .(99) The differentiation between arterial and venous blood flow disturbances is difficult

with.(100) . Heller reported that LDF can be used for as a reliable method for monitoring of free flaps which improves flap salvage rates once artifacts are ruled out.(101)

5) Single photon emission tomography

Single photon emission tomography (SPET) is a nuclear imaging technique as is PET. SPET uses tracers labeled with gamma emitting isotopes. Single photons are detected by a gamma camera instead of coincidence pairs, as in PET. SPET utilizes one-, two or three-headed gamma cameras rather than ring-detectors, as PET. Thus, SPET is less sensitive than PET, but less costly and more widely available, since it utilizes generator-based isotopes with long half lives (e.g. 99mTc T½ = 6 h) and on-line cyclotrons are not required. Since 1994, the addition of the coincidence detection mode to the detector system has enabled imaging of positron emitting tracers with gamma cameras as well.(102)

Single photon emission computed tomography (SPECT) has been used in the evaluation of bone revascularization of microvascularized fibular grafts for mandibular reconstruction.(103) However, the perfusion results attained are only semiquantitative and thus absolute values are not available using this method.

6) Dynamic computed tomography

Dynamic computed tomography (CT) is an imaging method in which a rapid sequence of images is accrued while a contrast medium, which typically contains iodine, is injected intravenously to the patient. The spatial resolution of the images is high and the signal intensity is in linear relation to the concentration of iodine. As the tracer flows through an organ, there is a short period of time before venous outflow begins and at this moment the amount of tracer is the highest in the organ tissue. Perfusion can be calculated as the ratio of the slope of the tissue time

density curve to the peak arterial density (104) Numerical values have been calculated rather than plain ratios(105)(106)(107)

Nevertheless, the concentrations cannot be exactly measured and thus the results should be regarded at the most as semiquantitative. Dynamic CT has been used to study perfusion in brain tumors.(108), head and neck cancer.(105)(106)(107) and lymphomas, where it is associated with grade (low grade vs. intermediate or high-grade).(109) Increased arterial perfusion in the liver in dynamic CT studies is a predictor of hepatic metastases.(110)(111) The maximum attenuation value in CT correlates positively with vascular endothelial growth factor staining of the tumor.(112)(113)

Gaggl et al studied perfusion-CT scans in 38 LD flaps in patients as predictors of postoperative ischemia. Among the recent-generation angiographic diagnostic techniques, multislice-CT has emerged as an outstanding noninvasive method for monitoring flap perfusion and also help in preoperative planning by to locating site of vessel preoperatively.(114)

7) Dynamic magnetic resonance imaging

Dynamic magnetic resonance imaging (MRI) can be used as a non-invasive method for evaluation of tissue perfusion. A concentrated bolus of a paramagnetic contrast agent needs to be administered to the patient. The contrast agent is usually a gadolinium chelate, gadopentetate dimeglumine. The signal produced by gadolinium depends on blood flow and vessel permeability, since the contrast agent passes into the interstitial space in substantial amounts. Sequential images are acquired from the area of interest following the intravenous injection of the contrast agent. For moving structures, such as the lungs, breath-held imaging is required.(104) This method provides only relative, not absolute, quantification of perfusion.(115) Dynamic CT and dynamic MRI data correlate well with each other (116) Dynamic MRI data

correspond also well with quantitative blood flow measured with PET.(117) However, the results of the MRI scan can only be interpreted as semiquantitative. In addition, MRI scanners with enclosed magnetic coils are of limited space, which limits the usefulness in e.g. large patients, or anesthesized patients, or in patients otherwise in need of close monitoring.

8) Temperature monitoring

Thermography is easy, inexpensive, and non-invasive. It has been used for mapping cutaneous perforators pre-, intra-, and postoperatively, and for monitoring the flaps bedside.(118)(119) Implantable thermocouple probe is fixed proximal and distal to the arterial anastomosis which will detect change in temperature difference after arterial occlusion. Reoperation was indicated if there was a temperature difference of more than 0.30 °C for more than 1 h.(119) Furthermore, the adequacy of tissue perfusion can be assessed via surface temperature recordings.(120) On the other hand, Kaufman reported in a small study that temperature monitoring is unreliable and nonreproducible.(121) In experimental studies, the measurement of collected venous drainage has been used to estimate flap tissue perfusion. Crabb determined flap blood flow gravimetrically as milliliters of blood per 5 min collected from the brachial vein.(122)

9) Pulse oximetry measures the percentage of oxygen saturation of hemoglobin. The principle is to transmit two separate wavelengths of light to distinguish between oxygenated and deoxygenated hemoglobin by light absorption differences. Menick successfully monitored postoperatively a revascularized free flap using pulse oxymetry on a cutaneous monitoring island flap in a latissimus dorsi muscle flap.(123) However, the movement of the sensor causes artifacts and the fixation of the probe to flap is difficult(60)

10) **Dilution techniques** are the commonly used to measure limb blood flow during exercise. Techniques are based on the infusion of indicator into blood and thereafter measuring its rate of dilution. The indicators must be fully mixed with the blood and they must not be retained or metabolized.

11) Plethysmography

One of the primitive methods to measure organ blood flow (Brodie and Russell 1905). It is based on measuring volume changes of the object, e.g. limb after venous outflow of the limb is occluded by a cuff. S

tack used reflectance photoplethysmography for monitoring 30 free flaps. (Stack et al. 2003). On the other hand, new methods studied by Chuah are not dependent on venous occlusion and produce more consistent results with or without hyperemia.(124)

12) Indo-cyanine green dye dilution and thermodilution are two of the most widespread methods. In dye dilution, blood flow is measured by continuously infusing dye of known concentration at a specific rate into the vessel (i.e. femoral artery). Simultaneously, the dye concentration is determined in the blood at the corresponding downstream vessel (i.e. femoral vein) and blood flow is calculated by a specific formula. In thermodilution, again, cold saline is infused instead of dye. During the steady state infusion temperature of the blood before infusion, the temperature of the infused saline and the temperature of the blood and saline mixture are measured. A specific formula is used to calculate blood flow.(87) The thermodilution method can be used for repetitive blood flow measurements in the tissue of interest because heat has no re-circulation problems, such as dye (125)(126)(127)(128) The drawbacks of the dilution methods include an invasive technique and the inability to measure regional blood flow.

13) Near-infrared spectroscopy (NIRS)??

This method is based on detecting light attenuation from dye (indocyanine green) infused into the tissue or from circulating oxygen**.** NIRS allows continuous measurement of concentration changes occurring in oxy- and deoxy-hemoglobin and oxidized cytochrome, the terminal enzyme of the respiratory chain and site of 90 % of oxygen consumption in the body.(129) The summation of oxy- and deoxy-hemoglobin reveals changes in total hemoglobin, reflecting changes in blood volume and providing an indirect indication of blood flow and perfusion**.** The oxygenation index is the difference between oxy- and deoxy-hemoglobin and reflects net changes in oxygenation independent of change in blood volume. Selective light absorption by oxygen-dependent tissue chromophores (hemoglobin) results in reduced light intensity**.** Attenuated optical signal exiting the tissue is analyzed using spectrophotometric principles that relate light absorption to the tissue concentration of the chromophore.(130) Characteristic absorption spectra of oxygenated and deoxygenated hemoglobin allow the system to calculate concentration of both hemoglobin forms.(131) NIRS measures hemoglobin content and oxygenation in all small-diameter vascular compartments of tissue (arterioles, venules and capillaries) and of vessels of larger caliber which absorb the light completely.

The values reported by NIRS monitoring reflect changes in the skin and subcutaneous fat tissues of cutaneous flaps.

Any dislocation of probe position influences the measurement considerably (132)(133). This inherent variability seriously obstructs any reasonable standardization of NIRS threshold values which would reliably indicate an imminent threat to flap. For this reason, it is recommended to observe the trends of NIRS parameter changes rather than absolute values (Repez et al. 2008).(16) One of its main advantages when compared to other noninvasive modalities is the

capacity of near-infrared light to penetrate to a considerable depth of tissue and to provide data on microcirculatory events occurring in a comparatively large volume of tissues.(134)(135) Conversely, laser Doppler flowmetry is limited to observing relatively superficial (1-2 mm) cutaneous circulatory phenomena susceptible to changes in local environment and microvascular heterogeneity. (136) A rather important drawback of NIRS monitoring is cost which is unjustifiable for departments with a low volume of flap reconstructions (Repez et al. 2008).(16)

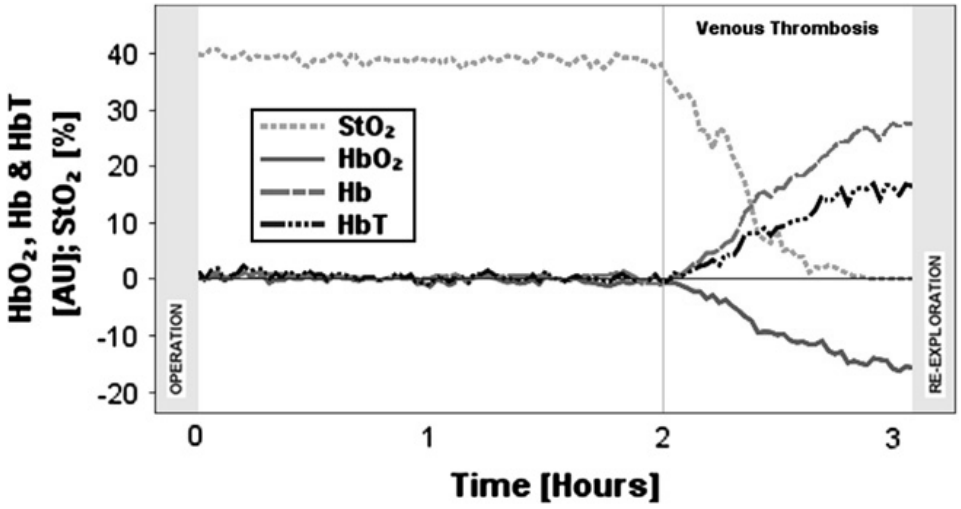


Figure9. Characteristic changes in NIRS parameters due to postoperative venous thrombosis

14) Electromagnetic flowmetry

Quantitative blood flow can be measured by by electromagnetic flowmetry in a Quantitative manner.(137) In this technique and electrodes placed on either sides of the vessel will measures electrical voltage proportional to the rate of blood flow is generated between the two electrodes (Guyton and Hall 2006).(24) Beekman studied the resolution of microvascular

vasoconstriction using an electromagnetic perivascular flow sensor.(138) Though electromagnetic flowmetry is a method that provides immediate, continuous, and quantitative measurement of blood flow, high technical standards, exact probe placement, and the requirement for electrogel around the vessel reduce clinical applicability.

15) Intravital microscopy

Intravital microscopy is an old method to study microcirculation. It is based on direct visualization (Figure 10). Ichioka studied the effects of amrinone on microcirculation.(139) They measured the diameters of individual microvessels of rats for quantification of microcirculatory blood flow. Also videomicroscopy and direct microscopic measurements have been used to study the vasodilating capacity of pharmacological agents.

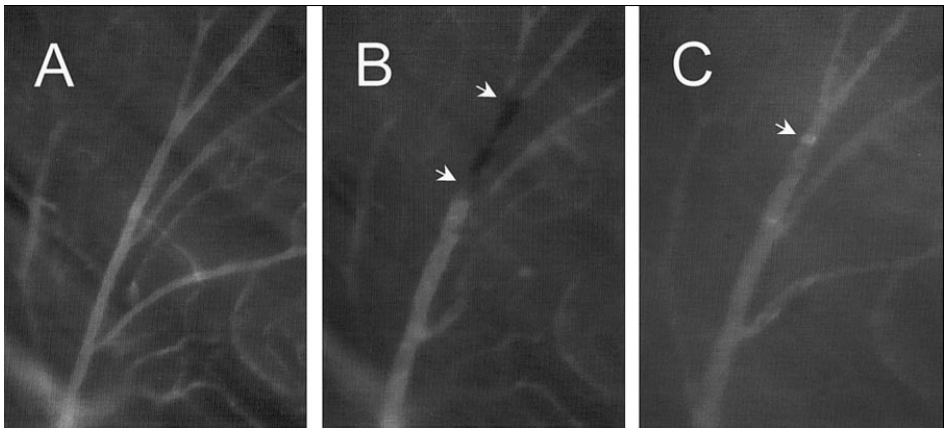


Figure 10. Intravital fluorescence microscopy of a thromboembolus arrested in a transverse arteriole in an osteomyocutaneous experimental flap. **A-** The transverse arteriole was stained with fluorescein-labeled dextran immediately before embolization. **B-** Thromboembolus arrested in the same arteriole visualized by negative contrast (arrows) using the blue filter combination and **C** by rhodamine staining of the platelets using the green filter combination.Magnification x 70.(140)

The major advantage for microcirculatory assessment is that the microscopic technique is direct and therefore allows in vivo visualization of individual microvessels.(141) The method cannot be used to study buried flaps. Oxygen measurements are independent on tissue dye concentration and optimal for detecting hypoxia, because the decay time is inversely proportional to the *p*O2 level.(142)

16) Positron emission tomography (PET)

PET is a functional imaging method that enables in vivo measurement of physiological and biochemical processes noninvasively and quantitatively. The radionuclides used in PET have a nuclear imbalance, i.e. an excess of protons. To restore the stability of the radioactive nucleus an extra proton is converted into a neutron and a positron is emitted. After travelling a short distance of 3-5 millimeters, the speed of the positron slows down and it collides with a nearby electron. Annihilation occurs, since positrons and electrons are antiparticles of each other. The mass of these particles is converted into energy in the form of two gamma rays, i.e. photons that travel in opposite directions. The PET scanner detects the two simultaneous (coincident) gamma rays from the annihilation site by detectors that are arranged in a ring-shaped pattern around the patient. An image can be reconstructed after a sufficient number of coincident gamma rays (counts) have been detected. The distance that the positron travels before annihilation depends on its energy, which is specific to the radionuclide. The resolution of the PET image is determined by the design of the PET scanner, the radionuclide, and the processing of data during reconstruction. To achieve quantitative measures several corrections need to be applied, e.g., tissue attenuation, scattering gamma rays, random counts and dead time losses.(143) The compounds labeled with a positron-emitting radionuclide are injected into a patient. The most common PET radionuclides have a short half-life. This moderates the radiation dose to the

patient, which is comparable to a CT study of the abdomen, i.e. approximately 1-3 milliSieverts. Typical radionuclides used are fluorine (18F), carbon (11C), nitrogen (13N) and, oxygen (150) with the respective half-lives 109.8 min, 20.4 min, 10.0 min and 2.05 min(144).

17) Oxygen-15 labeled water

Oxygen-15 labeled water ([15O] H2O) is a chemically and metabolically inert tracer used to assess tissue perfusion**.** It is freely diffusible and has a short radioactive halflife (T½ = 2.05 min or 123 s), allowing repeated measurements. The method is based on the difference between arterial blood activity and the activity in the tissue of interest. However, this difference diminishes in very high flow rates, and under these conditions the method becomes less reliable.(145) [15O] H2O is administered to the subject usually intravenously as an infusion or as a bolus**.** This tracer can be studied also by letting the subject inhale oxygen-15 labeled carbon dioxide ([15O] CO2), which is rapidly converted in the lungs to [15O] water by carbonic anhydrase, producing arterial input of [15O] water. By continuous inhalation a steady state of radioactivity can be reached in the tissues. By measuring the activity level in arterial blood during inhalation of [15O] CO2, quantitative values can be obtained. Estimates of tissue uptake can be obtained roughly either by calculating the target-tonormal tissue ratio, or by measuring the standardized uptake value (SUV)**.**

18) Flap Capillary Glucose monitoring using Glucometer

The first instrument to give quantitative analysis of blood glucose was developed by Anton Clemens in late 1960s. (146)

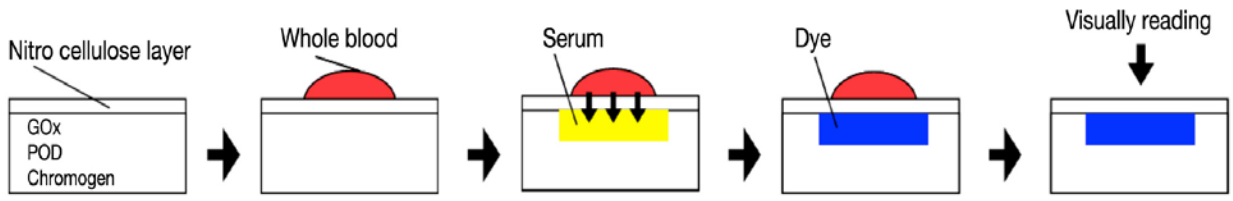
SMBG Systems Based on the Colorimetric Principle-(147) Dr Free from Miles Laboratories Inc. developed the first blood glucose test strips based on the colorimetric method in 1960s The

preparation of strips was done by using filter paper which was dipped in an solution containing glucose oxidase (GOx), peroxidase, and chromogen. After drying the paper it was dipped in a solution of nitrocellulose solution which forms a semipermeable membrane. This semipermeable membrane allows only passage of serum glucose into the reagent layer while blocking passage of blood cells. (148)

$$\text{Glucose} + O_2 \xrightarrow{\text{Glucose oxidase}} \text{Gluconic acid} + H_2O_2$$

$$\text{Chromogen} + H_2O_2 \xrightarrow{\text{Peroxidase}} \text{Dye}$$

Reaction principle

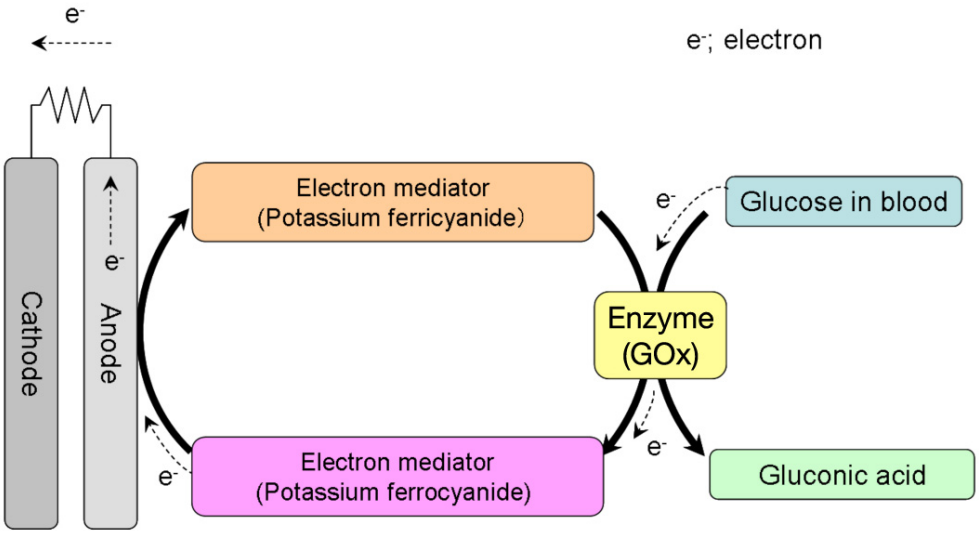


Structure of the Dextrostix test strip.

SMBG System Based on the Electrochemical Principle--(147)

.A disposable blood glucose test strip using a GOx and electron mediator mixture placed upon an electrode substrate was made by Genetics International (established in Inverness, United Kingdom), The test strip was then measured by a handheld, pen-shaped device capable of detecting the small current signal that was generated, which corresponds to the concentration of glucose in the sample. (149)

In this process a disposable test strip was placed at the tip of the device and 10 µl of blood from a finger tip was applied. This generates hydrogen peroxide from the catalytic GOx. Hydrogen peroxide was detected by the electrode and converted into a whole blood glucose concentration and displayed on the screen located on the side of the device.(150)



The principle used in the disposable test strip based on the Electrochemical Principle

In 1996, Roche released it's the first biosensor blood glucose meter was released by Roche in 1996 named Accu Chek Advantage, which utilised GDH and the coenzyme pyrroloquinoline quinone (PQQ).

Although more sensitive than the glucose oxidase reaction, it was prone to interference by high concentrations of maltose or galactose.(151)

Setalare et al. found that the blood glucose level in flaps is reduced in ischemic or congestive conditions by using microdialysis.(15) Interstitial glucose monitoring is highly sensitive and

specific for vessel occlusion and offers a rapid, inexpensive, and accurate method of flap monitoring. (152)

Sakakibara et al. was first to report use of glucometer as a monitoring tool for flap perfusion and suggested that a lower blood glucose level is indicative of flap ischemia in clinical cases.(153) H. Hara also monitored flap blood glucose measurement in post operative period by using glucometer. (154)

Glucometer provides easy and fast blood glucose estimation and produces quick result within 5 seconds. It requires tiny sample size <0.6 µL with under dosing detection. Glucometer compensates for temperature variables and Performs at temperatures from 8oC to 44oC.

Glucometer may provide false results in few situations like critically ill patients, Poor perfusion due to hypotension, High oxygen tension in patients receiving oxygen therapy, Low pH (<6.95) and Extremes of Temperatre and Humidity.(155)

A number of factors can affect the accuracy of glucose meter results, including operator technique, environmental exposure, and patient physiologic and medication effects.

Flap failure

Flap failure occurs clinically with devastating consequences. Siemionow reported that the initial 3 days following microvascular procedures are the most critical ones for tissue survival.(156) Complications prolong the median hospital stay of these patients by 7.5 days. Flap failure correlated with the rate of preoperative infections of the recipient site and with prolonged operation time. (157)**.** Sasmor suggests that the flap failure rate increases by recipient site in the following order: upper extremity, breast, head and neck, and lower extremity(26).

Failure of a skin flap has been attributed to either intrinsic or extrinsic causes. The extrinsic factors include systemic conditions (e.g. infection, atherosclerosis, hypotension, and

malnutrition) and local causes (e.g. compression, tension, thrombosis of the anastomoses, kinking of a pedicle and inadequate nutrient blood flow within the skin flap. (158)

Flap ischemia and reperfusion injury

Flap survival requires sufficient tissue perfusion. If this fails, hypoxia and waste products induce harmful effects to the flap. Two types of ischemic injury are possible: distal ischemia or global ischemia. Global ischemia is a consequence of obstruction in arteries or veins of the pedicle. Distal ischemia might develop by inadequate flap design**;** the flap may be too large in relation to feeding vessels, which subjects the edges of the flap to ischemia**.** On the other hand, even with impeccable flap design and flawless surgical technique, partial or total flap necrosis is possible. Therefore, an improved understanding of global flap hemodynamics and the response of the flap to compromised perfusion are fundamental for successful surgery.(159)(160)

The primary critical ischemia time is maximum length of time that vital tissue can tolerate complete ischemia and yet remain viable once circulation is restored**.**(161) Secondary ischemia occurs, if a postoperative complication reduces flap circulation. Compromised venous BF is more detrimental to flap survival than arterial ischemia(160) The average primary and secondary critical ischemia times of cutaneous flaps are 13.1 hours.(159)(161) and 7.2 hours respectively (159)**.** Here, average means that 50 percent of the flaps are lost if this time is not kept. Thus, cutaneous flaps are more vulnerable to secondary ischemia than to primary ischemia. The primary and secondary critical ischemia times of musculocutaneous flaps are 9.1 hours and 11.3 hours, respectively**.**(162) Therefore, muscle tissue adapts better to secondary ischemia, possibly due to stimulated anaerobic metabolism**.** It is fair to state, however, that the difference in the tolerance of ischemia and in the response to ischemia between skin and myocutaneous flaps has not been confirmed. Picard-Ami found a statistically significant decrease in survival of both skin

and myocutaneous flaps after 6 and 8 hours of ischemia, respectively.(163) In practice, skin tolerates ischemia better than muscle tissue**.** Restoration of blood flow in ischemic causes further tissue damage.(164) Anaerobic metabolism generates a variety of noxious substances during the period of ischemia (Figure 11). A flap subjected to global ischemia is damaged not only by the period of hypoxia, but also by the reperfusion period, when many of these substances are further metabolized, and toxic free radicals are generated**.** The production of the toxic substances can proceed for 24-48 hours after reestablishment of perfusion.(38) These toxic free radicals may cause peroxidation of cellular and intracellular membranes and intracellular proteins, resulting in irreversible cell injury(5)(38) (Figures 11- 12**).** Exposure of endothelial cell membranes to free oxygen radicals results in increased permeability, leading to edema and hemorrhage, and to exposure of collagen and basement membranes; this promotes platelet and granulocyte adhesion and initiates a cascade leading to microvascular thrombosis (6). Increased vascular resistance and decreased blood flow rates further enhance platelet adhesion and thrombosis in the flap.(26) The extent of this phenomenon, called ischemia-induced reperfusion injury, is related to the duration of ischemia(165).

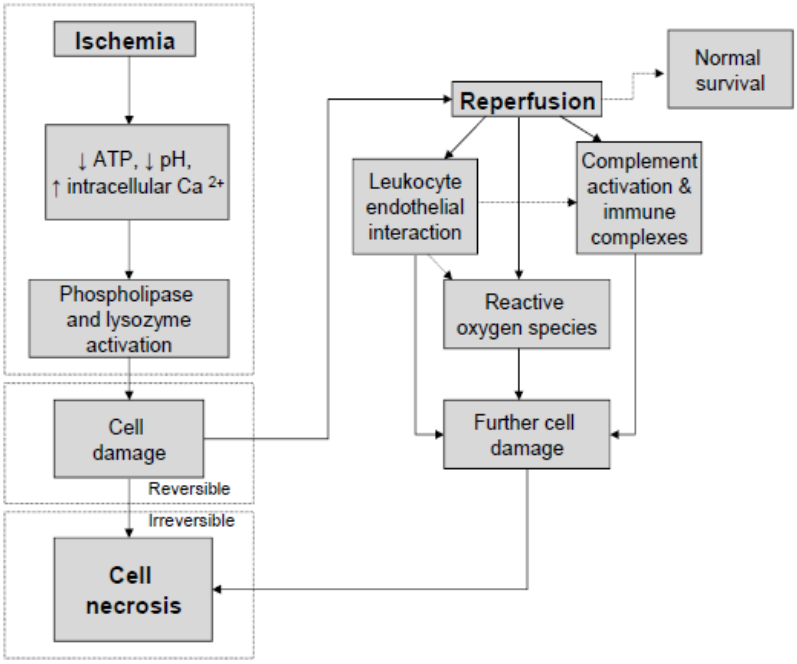


Figure11.Sequence of events during ischemia and reperfusion.

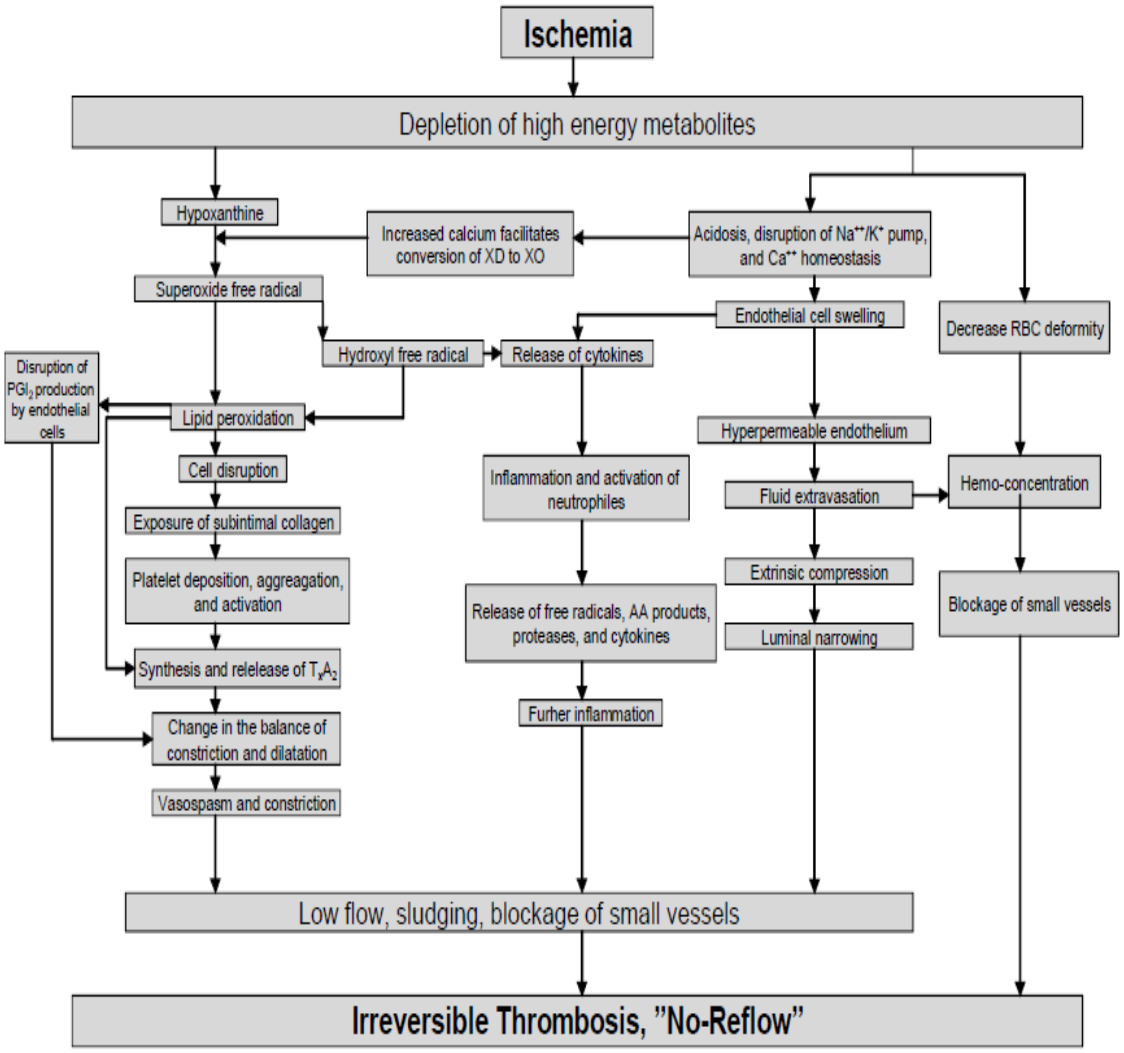


Figure12. Proposed interconnected mechanisms of reflow.

ATP = adenosine triphosphate; XD= xanthine dehydrogenase; XO = xanthine oxidase; Na+ = sodium; K+ = potassium; Ca2+ = calcium; RBC = red blood cell; PGI2 = prostacyclin (prostaglandin I2 [PGI2]); TxA2 = thromboxane A2.(Calhoun et al. 1999**).**

Prolonged ischemia induces stepwise catabolism of ATP to hypoxanthine, and xanthine oxidase activity increases**.**(166) Xanthine oxidase (XO) generates superoxide (O2 -) in the presence off

hypoxanthine during reperfusion**.** Interaction of O2 - with hydrogen peroxide (H2O2) in the presence of a transitional metal (e.g. iron) generates hydroxyl radicals (OH-) which are extremely cytotoxic (38)(6) The xanthine oxidase activity correlates well with the fate of free flaps.(166). Also other sources of oxy-radicals contribute to ischemia-induced reperfusion injury. A major part of the O2 consumed by activated neutrophils is converted to O2 - by membraneassociated nicotinamide adenine dinucleotide phosphate (NADPH) oxidase**.** The O2- is further converted to H2O2 and OH- as described above. Also, myeloperoxidase in neutrophils catalyzes the conversion of H2O2 to hypochlorous acid, which is also a potent cytotoxic oxidizing agent. Cordeiro used L-arginine to reduce the neutrophil counts, which did reduce neutrophil-mediated tissue injury.(167) Vascular spasms during surgery are a well-known phenomenon. They may lead to loss of transplanted tissue. Vascular spasms are associated with ischemia, interstitial edema, tissue temperature, acidosis, metabolic derangement, and humoral or neural vasoactive substances(36). In addition, there are physiological and mechanical factors associated with vasospasm. For example, blood-induced segmental vasospasm has been identified **,**(168) and an artery might constrict due to the myogenic response to stretching of the artery wall. A metabolically induced vasospasm may be induced by local vessel injury through damage to the endotheliumof the artery**.** This would induce vasospasm in the damaged segment through depletion of prostacyclin and other nonprostaglandin vasodilators. Local vasoconstrictors, like endothelin-1, which is a potent vasoconstrictor released by vascular endothelium, and thromboxane A2, a short-lived vasoconstrictor released from the circulating platelets, may also become activated during and after microsurgery.(36)(46)

Material and Methods

Material and Methods

At CMC hospital Vellore, All patients who underwent pedicled flap and free tissue transfer in Department of Plastic Surgery were assessed post operatively and followed up to 5th post operative day. The clinical examination was standardized with skin paddle color, temperature, skin reperfusion time, and bleeding test with a prick. Flap capillary glucose levels were measured by pricking the distal part of flap and measuring glucose levels of flap by glucometer. Examination was done postoperatively hourly for first six hours, then every 6th hour thereafter for next five days. A routine baseline capillary glucose level measurement was also done in all patients**.** Data was collected to analyze efficacy of capillary glucose measurement of flap for post operative monitoring.

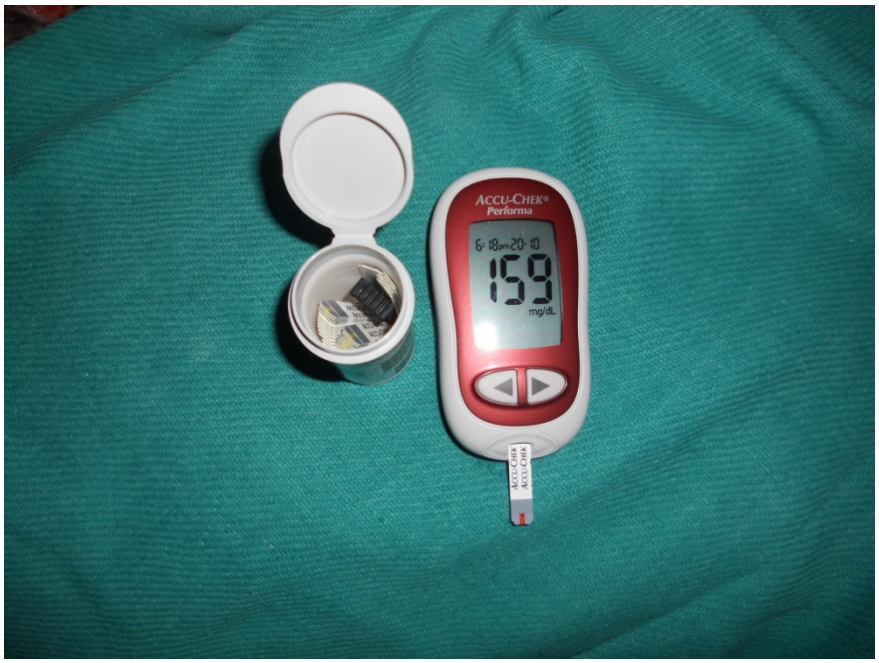
Inclusion criteria: All patients undergoing pedicled/free flap surgery. Diabetic patients will be studied as a separate subgroup.

Exclusion criteria: All patients with buried flap.

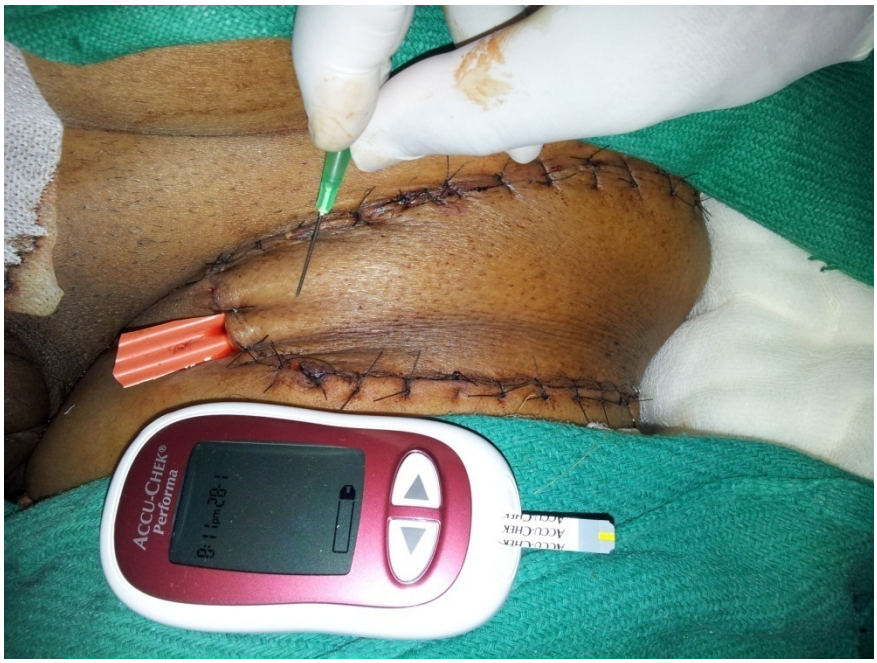
The diagnosis of flap failure is according to the clinical features. (Described by Mathes and Nahai) Flap with pale colour, without Capillary refill or dusky flap with exceptionally brisk refill, dark purplish ooze, cold on touch are features of failing flap. (Ref. Plastic Surgery - volume 1 general principals, Page No 496, 497) Diagnosis of flap necrosis was made by senior plastic surgeon.

Normal value of blood sugar in adult: 80-120 mg/ml. Values in flap should be as that of normal blood sugar levels. Flap glucose measurements were done on the patients undergoing reconstruction with flap. Flap capillary glucose levels decreases in

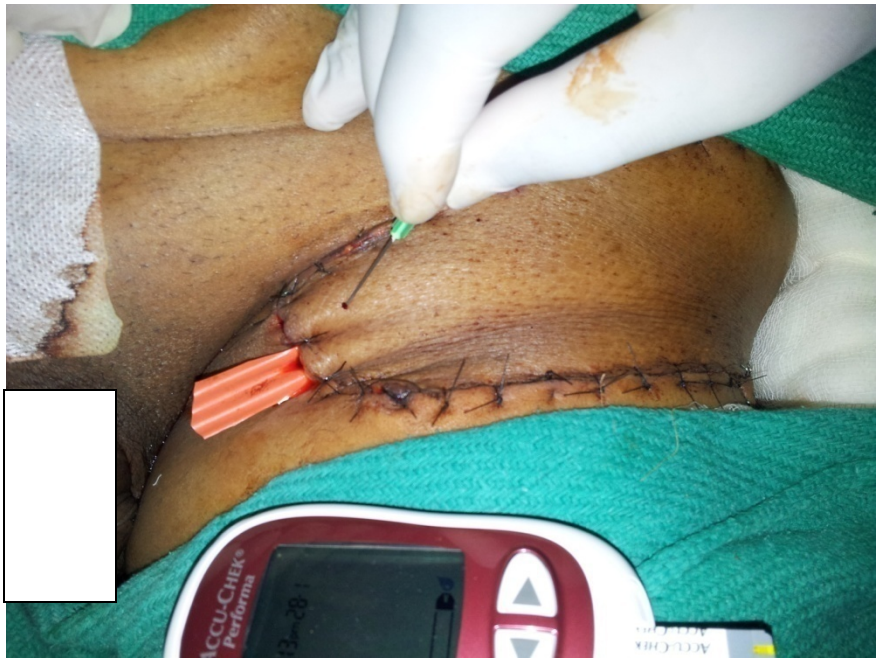
compromised/failed flaps. As flap capillary glucose is considered as the possible marker of flap failure, we expect it to be decreased in ischemic flaps and should be normal if there is no ischemia. To minimize bias person doing glucose monitoring test will not make the diagnosis of flap failure. Quantitative data was expressed in frequency and percentage. Data was expressed as mean value and standard deviation (SD) for capillary glucose levels in flap. Diagnostic accuracy measuring sensitivity and specificity was calculated with 95% confidence interval. In order to decide the best cut-off value ROC curve was plotted with clinically assessed tissue as survived or failure. These findings were tabulated against glucose monitored value. Flap capillary levels at every 6th hour was arranged for survived and failure cases and ROC curve was plotted. The best of all this ROC was identified and best cut-off value of blood sugar for this ROC was selected. Collected Data was divided in to two groups, i.e. Values noted in patient with flap survival and in patients with flap failure. Correlation of the flap glucose value was done to assess the diagnostic validity of the test.



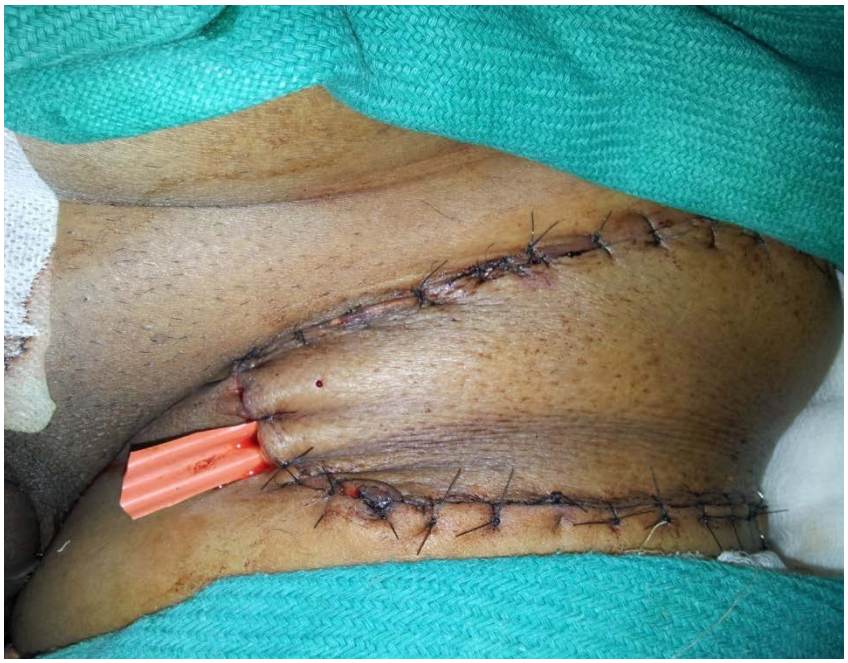
1) Glucometer and Sugar strips



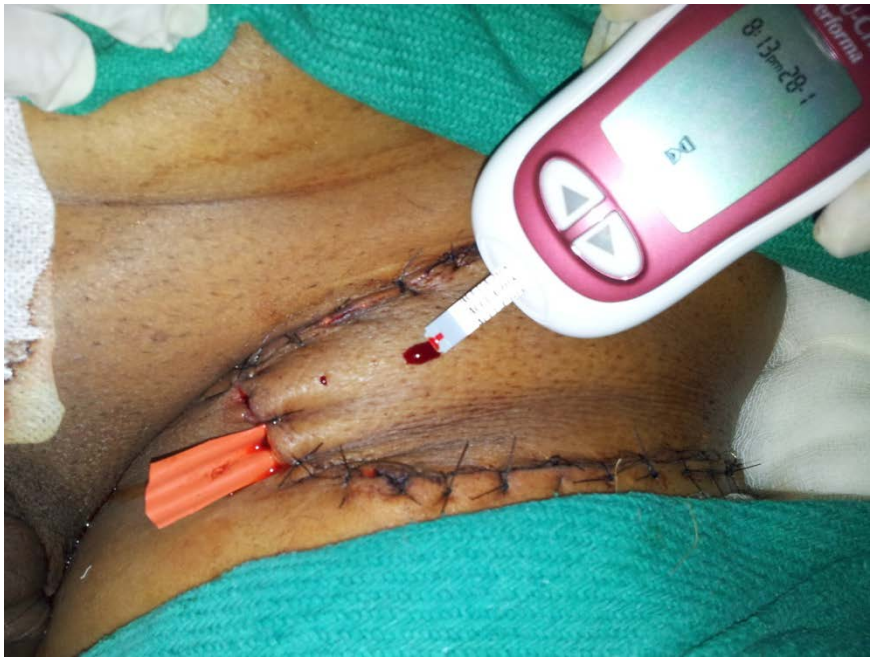
2) Pricking the distal part of flap



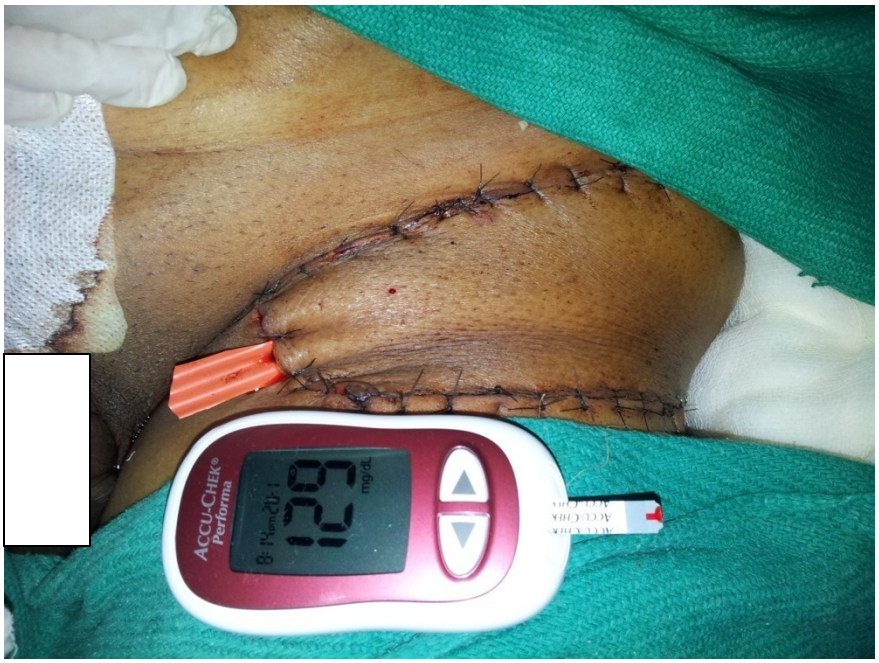
3) Pricking the distal part of flap



4) Bleeding point from the distal part of flap



5) Measuring Capillary Glucose levels of Flap by Glucometer



6) Normal level of Flap Capillary sugar levels indicating healthy flap

Results and Analysis

Results and Analysis

A total of 60 patients were included in study with mean age of 41.4 years.

Among them 77 % were males and 23 % were females.

Out of these 27 flaps were done for defects related to trauma, 26 flaps were done for oncological defects, 5 flaps were done for burn reconstruction and one flap was done for leprosy nose reconstruction.

There were 38 pedicled axial flaps, and 13 random pattern flaps and 9 free flaps.

Out of 60 flaps 42 flaps survived fully without any complication, while There was minor distal necrosis in 11 flaps and major partial necrosis was seen in four flaps (two reverse sural artery flap and two random pattern flaps.

Complete flap loss was seen in 3 patients (two free flaps and one pedicled axial flap).

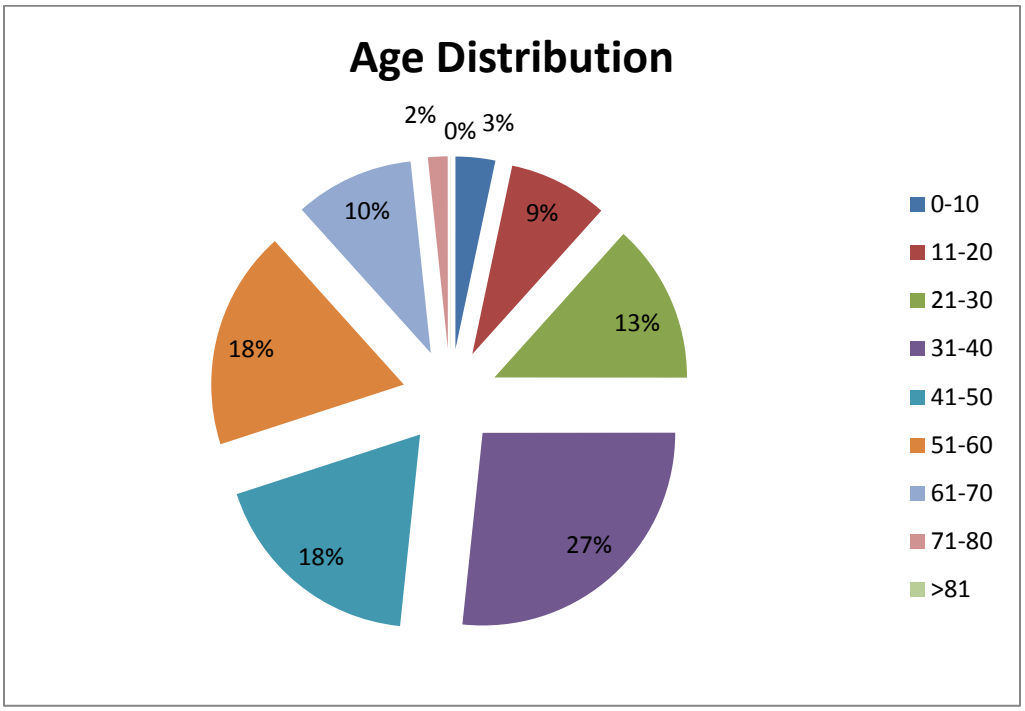
Two patients were diabetic**.** Flap of both diabetic patients survived and there flap sugar levels were higher than normal and it was correlating with the blood sugar levels.

1) DEMOGRAPHIC PROILE

TABLE: 1

Age Group(In years)	N= 58	Percentage (%)
0-10	02	03
11-20	05	08
21-30	08	14
31-40	15	26
41-50	11	19
51-60	11	19
61-70	05	09
71-80	01	02
>80	00	00

FIGURE: 1.

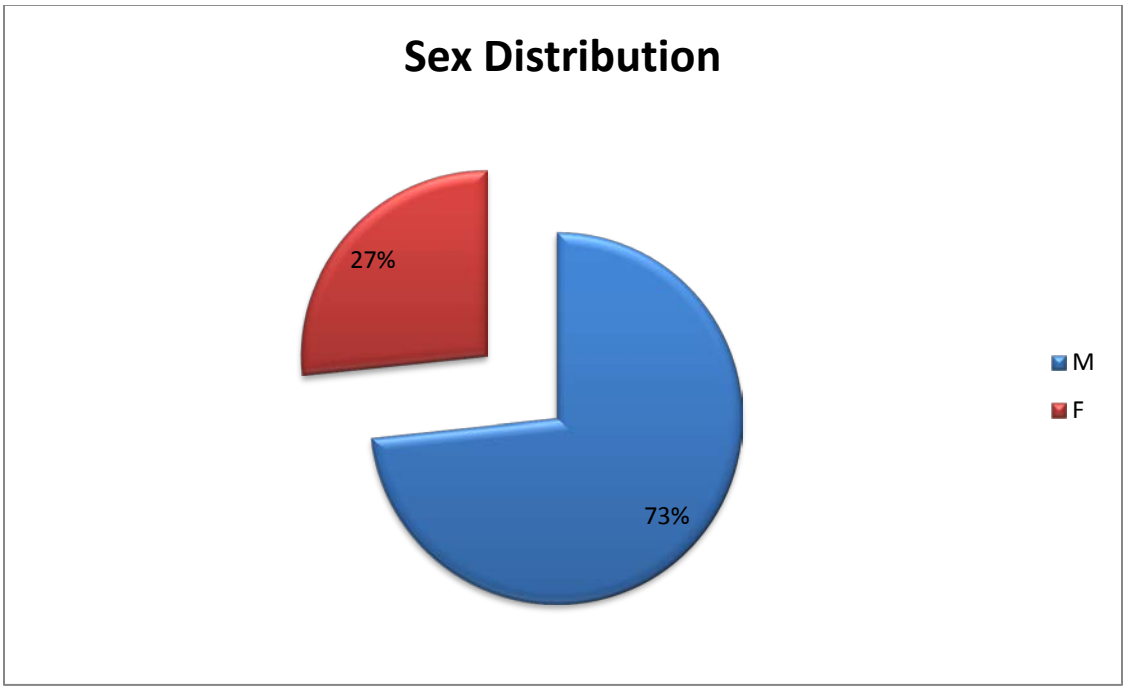


2) SEX DISTRIBUTION

TABLE: 2

Sex	Number	Percentage
Male	44	73
Female	16	27

FIGURE: 2

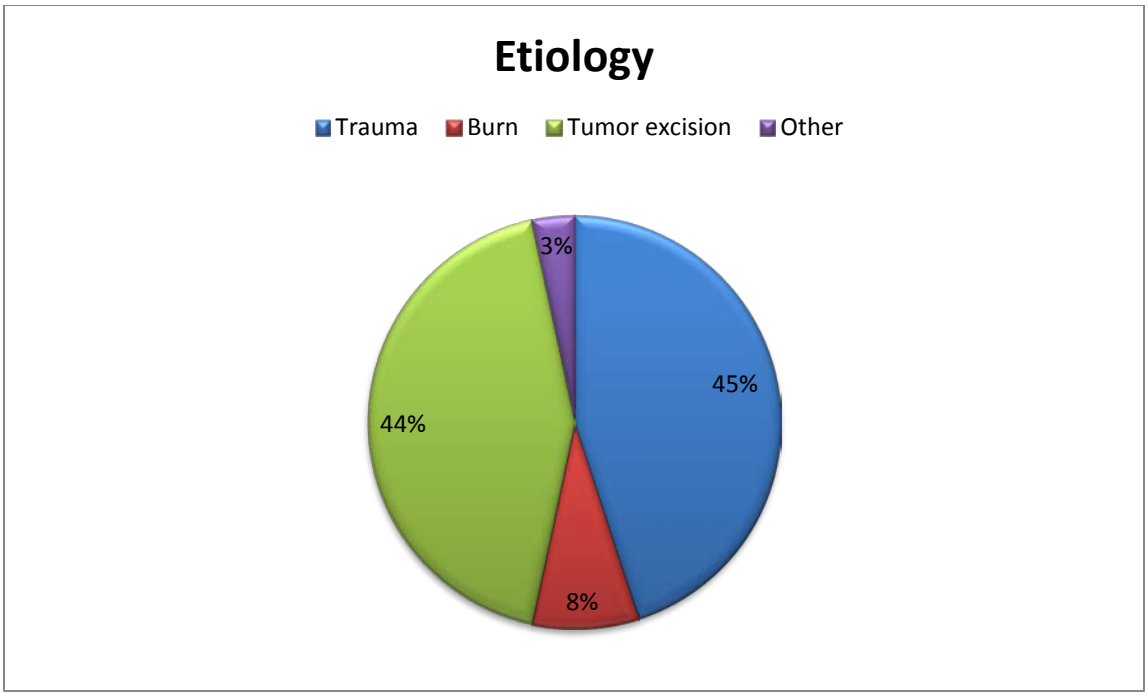


3) ETIOLOGY

TABLE: 3

Etiology	Numbers
Trauma	27
Oncological	26
Burn	5
Other	2

FIGURE: 3

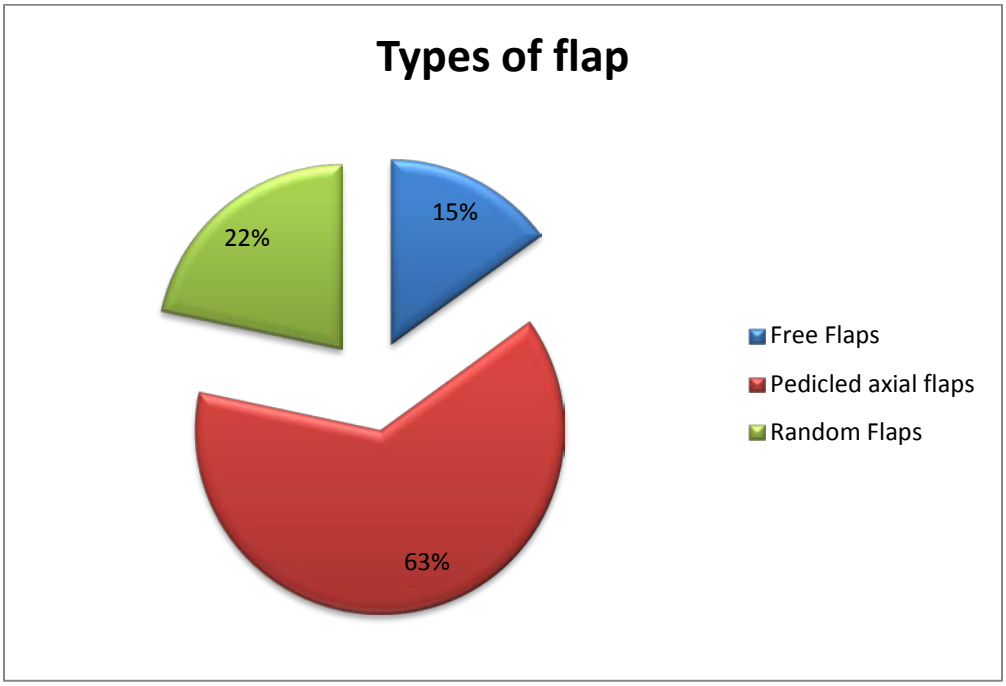


4) TYPES OF FLAP

TABLE: 4

Type of Flap	Numbers
Pedicled axial flaps	38
Random Flaps	13
Free Flaps	9

FIGURE: 4.1



5) COMPLICATION

TABLE: 5

Complication	Number of patients
Flaps survived fully	42
Minor Partial Necrosis	11
Major Partial Necrosis	4
Total Flap loss	3

FIGURE: 5.1

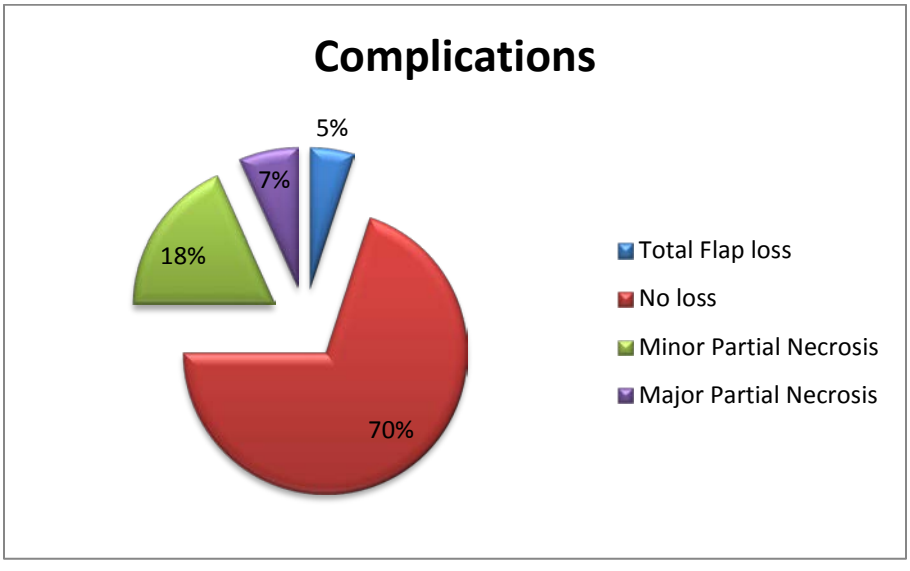


FIGURE: 6

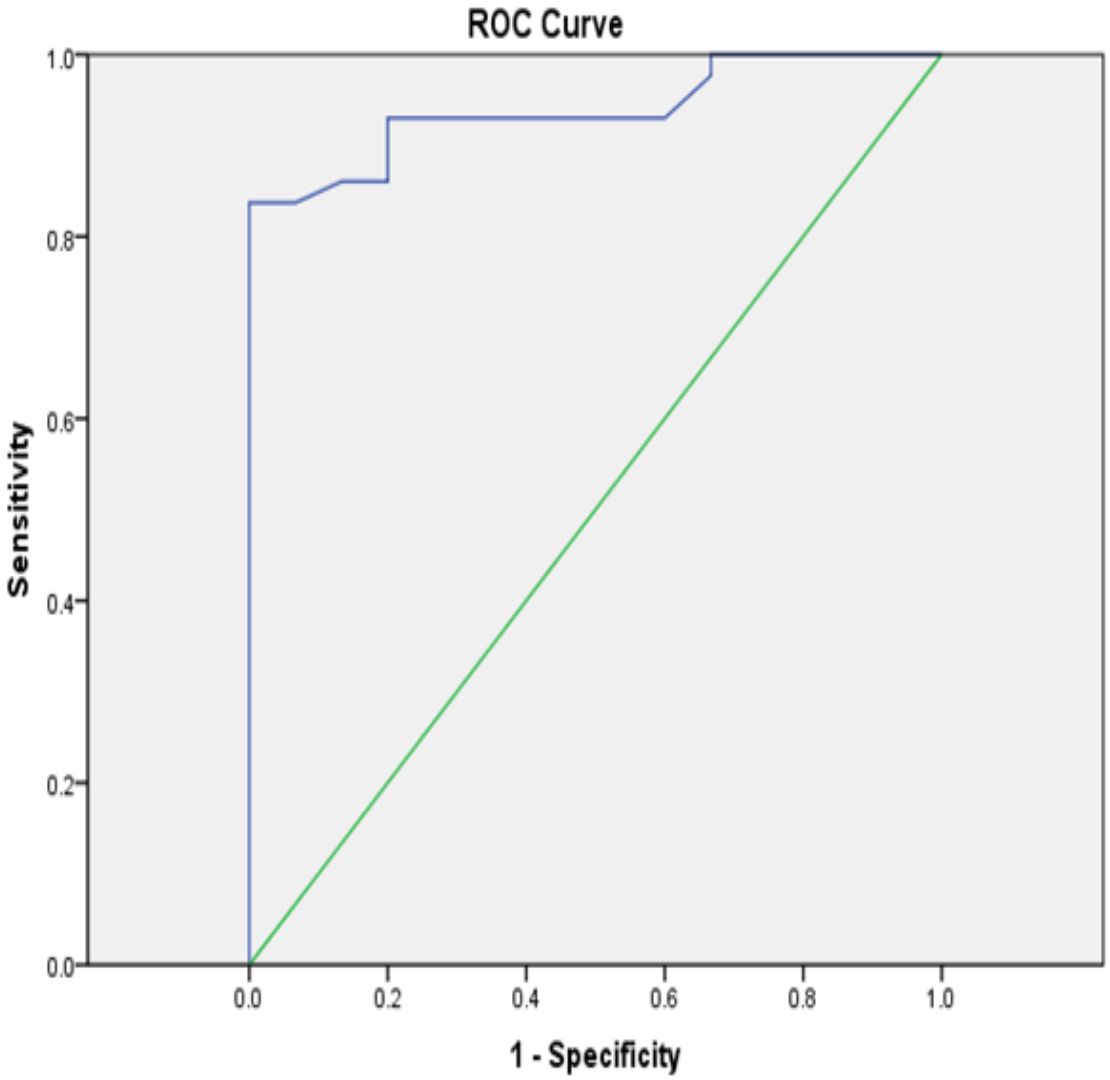


FIGURE: 6, Receiver operating characteristic curve (ROC) showing diagnostic performance of BGM for Flap Monitoring. (Y axis: Sensitivity, X axis: 1- Specificity)

For Each Flap Capillary glucose level plotted on ROC curve sensitivity and Specificity is calculated. The value which is plotted nearer to 1 i.e. value having highest sensitivity and specificity is the cut off value.

Table: 6

Area under the curve
0.939 (95% confidence interval)

Table: 7

Co-ordinates of Curve			
Value (mg/dl	**Sensitivity**	**Specificity**	**1- Specificity**
55	.930	.733	.267
61	.930	.800	.200
64	.907	.800	.200

The area under the ROC curve was 0.939 which indicates a strong relationship between flap capillary levels and Flap survival. Using ROC curve the co-ordinates of curve were determined. Flap capillary glucose value of 61 mg/dl was proposed as a cut off value for which the sensitivity was 93% and specificity was 80%. A value less than 61 mg/dl is suggestive of flap ischemia. Keeping cut off value as 61 mg/dl, cross tabulation was done to calculate PPV (Positive Predictive value) and NPV (Negative Predictive Value). Mean sugar values were significantly low in the non survival group on different times (Table-9, Figure-7). The mean flap sugar value for survival and non survival group it was 109mg/dl and 42.5 mg/dl respectively (Table-10). The flap BGM (Blood glucose measurement) gradually increases over a period of 4-6 hours and

achieves a steady state (figure-8). The flap sugar levels were low as compared to normal finger tip capillary sugar levels in case of free flaps which gradually increases over a period of time and equals that of finger tip capillary sugar levels over a period of 4-6 hours. But in pedicled and axial pattern flaps the levels were same as that of normal capillary sugar levels. There was an initial low sugar levels in 5 pedicled and random flaps which was not statistically significant. Chi-Square test was done to check the null hypothesis (The Distribution of Flap capillary glucose level is same in survived and non survived flaps). The p value was <0.5, which rejects the null hypothesis and indicates a strong relationship between low flap BGM and ischemia. (Table 11 &12)

Table: 8

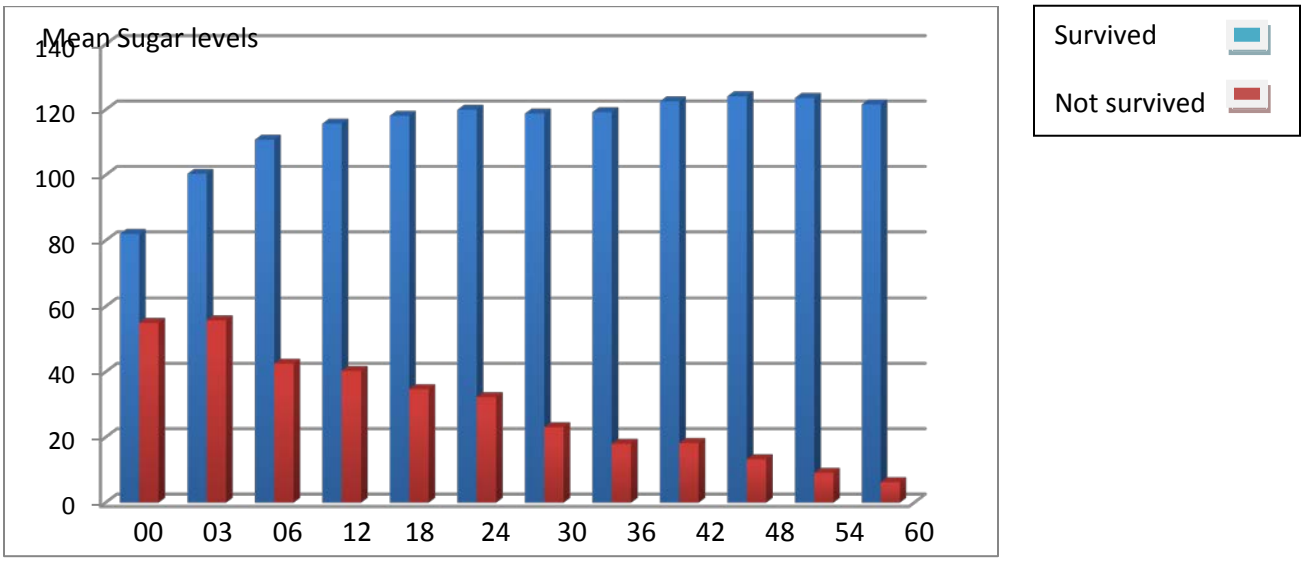
Sugar level Outcome Cross tabulation					
			Outcome		
			Survived	Not survived	Total
Sugar level	<61	Count	4	12	16
		% within Sugar level	20.0%	80.0%	100.0%
		% within Outcome	7.0%	80.0%	25.9%
	>61	Count	40	4	44
		% within Sugar level	93.0%	7.0%	100.0%
		% within Outcome	93.0%	20.0%	74.1%
Total		Count	44	16	60
		% within Sugar level	74.1%	25.9%	100.0%
		% within Outcome	100.0%	100.0%	100.0%

Table: 9

Timings (in Hours)	Mean Capillary Glucose levels in survived cases(mg/dl)	Mean Capillary Glucose levels in non survived cases (mg/dl)
0	82	55
3	100.4	55.8
6	110.83	42.5
12	115.76	40.31
18	118.17	34.73
24	120	32.27
30	118.83	23.07
36	119.26	18
42	122.57	18.25
48	124.14	13.27
54	123.62	9.11
60	**121.66**	**6.25**

Mean Capillary glucose levels in survived and not survived flaps

Figure: 7



Comparison of mean sugar values with time in survival and not survived flaps

Testing significance of Association

Table: 10

	Survived	Not Survived
Mean (mg/dl)	109.2	42.5
Median	113	43
SD	36.5	21.7
Min. Value (mg/dl)	46	0
Max. Value (mg/dl)	255	76

Comparison of Capillary glucose levels of Flaps

Figure: 8

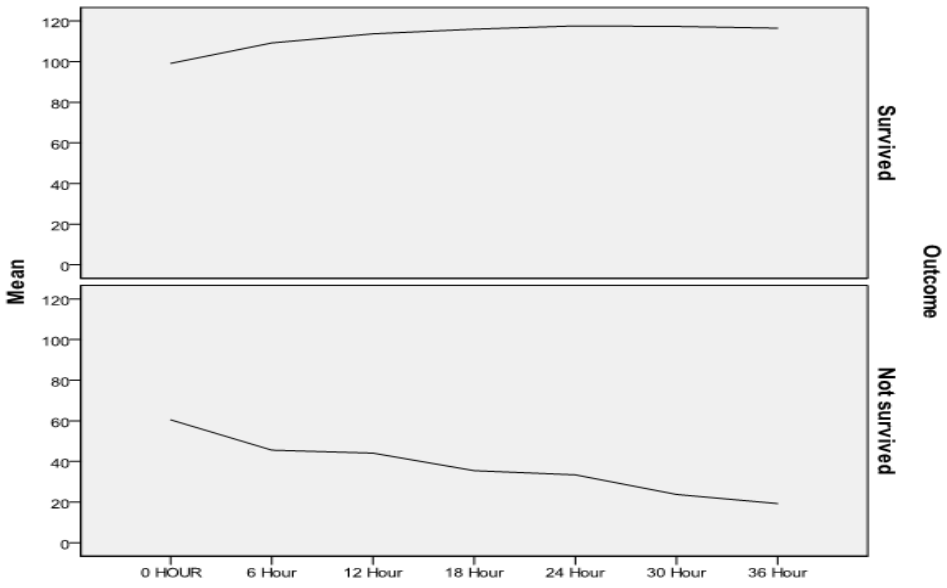
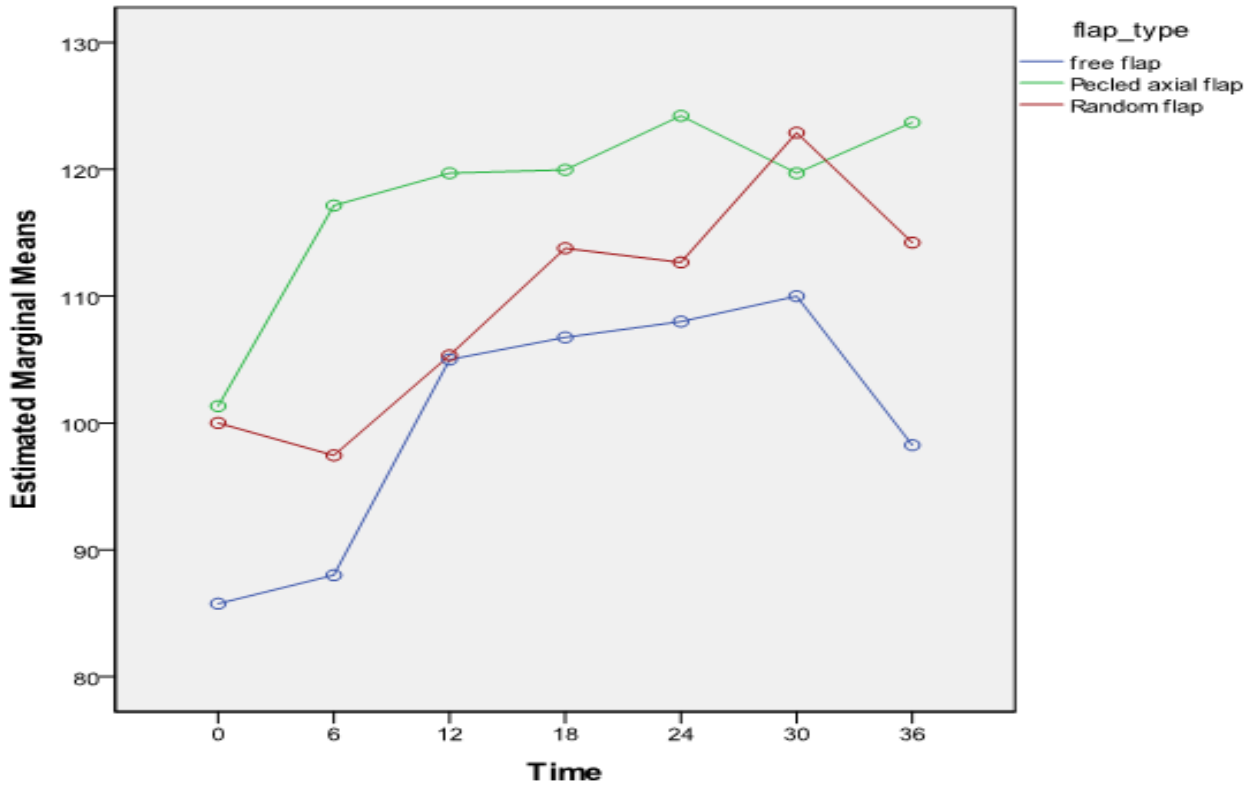


Fig: Change in sugar levels of flap over a period of time

Figure: 9



Change in sugar levels of flap over a period of time in different type of flaps

P value = 0.010(Greenhouse-Geisser test statistic is used to compare the values over different points.)

Chi-Square Test

Table 12

	Value	Df	Asymp. Sig.(2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	33.108[a]	1	.000		
Continuity Correction[b]	29.647	1	.000		
Likelihood Ratio	38.785	1	.000		
Fisher's Exact Test				.000	.000
Linear-by-Linear Association	32.537	1	.000		
N of Valid Cases	60				

a. 0 cells (.0%) have expected count less than 5. The minimum expected count is 5.69

b. Computed only for a 2x2 table

c. P Value = .001, which is less then < 0.05

Diagnostic performance of Test

Table: 13

Variable		Ischemic flap
Cut off value (mg/dl)		61
Sensitivity (%)		93
Specificity (%)		80
Positive Predictive Value (%)		0.88
Negative Predictive Value (%)		0.83
Area under the Curve		0.939
95% Confidence Level	Upper	0.997
	Lower	0.881

Discussion

Discussion

Flap surgery is a technique in plastic surgery where tissue from donor site is lifted and moved to a recipient site while keeping its blood supply intact. This procedure is done mainly to fill a defect such as a wound resulting from injury or surgery.

Flap monitoring via clinical observation of skin colour, capillary refill, and dermal bleeding remains the benchmark, but issues related to hospital staffing and to the difficulty of making a clinical determination of a flap's perfusion have hastened the search for more objective monitoring methods(71)(169). Methods that have been currently used include internal and external thermometry, laser Doppler flowmetry, internal and external Doppler monitoring, quantitative fluorescein fluorescence, pulse oximetry, and transcutaneous oxygen monitoring. The most popular of these methods are external Doppler monitoring, implantable Doppler monitoring, and assessment of coetaneous blood flow using laser Doppler flowmetry.(169) These tests are highly expensive and needs specialized setup and specialised personnel.

Interstitial glucose monitoring is highly sensitive and specific for vessel occlusion.(170) This technology offers a rapid, inexpensive, and accurate method of monitoring free tissue transfer[4]. In 2010, Sakakibara et al. reported a lower blood glucose level in congestive flaps in clinical cases[5](171). Setalare et al. found that the blood glucose level in flaps is reduced in ischemic or congestive conditions by using microdialysis(15)(93) H. Hara has described blood glucose measurement (BGM) in a flap over a period and the use of BGM for flap Monitoring[7](172). Hypothesis behind low Flap glucose levels in ischemic flap is still not clear. It is believed that there is raised capillary and venous pressure in ischemic flaps causing reduced blood flow entering to the flap. Due to the

reduced blood flow the supply of sugar to flap will be reduced and it will attain a state of hypoglycaemia. Hypoxic state of flap due to reduced blood flow will lead to anaerobic metabolism. Cells under an anaerobic metabolism do not consume oxygen, indicating low consumption of glucose and reduced flap BGM. Thus, a flap with vascular complications shows numerous metabolic changes that are monitored by an excellent method—microdialysis. The concentration of pyruvic acid and lactic acid increases after occlusion of pedicle vessels, and the anaerobic metabolism overcomes the aerobic metabolism.10,11 Although microdialysis shows excellent sensitivity and specificity, the instrument is very complicated and expensive and not possible to introduce into every hospital.

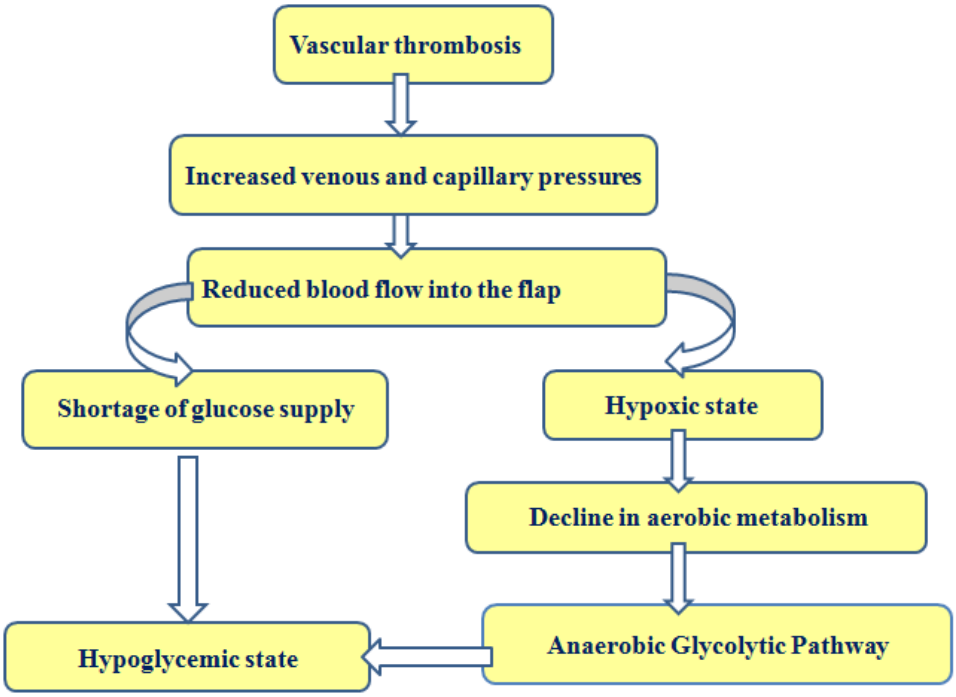


Fig: Mechanism involved in low sugar levels of ischemic flaps

Flap monitoring was done by measuring blood glucose levels using accu check performa glucometer (Fig 3), which is routinely used for regular capillary blood glucose

measurements. The procedure is rapid and simple and requires only minimal amounts of blood (06-10 μL). Furthermore, this method is more quantitative than the traditional ways of flap monitoring. In the current study, a cutoff value of 61 mg/dl is proposed for the BGM. For thiscut off value the sensitivity is 93% and specificity is 80%. A higher sensitivity would be better for more certain detection of venous thrombosis for flap salvage. However, the use of a higher Cut off value may lead to unnecessary re-exploration of flaps.

In the present study, the blood glucose level showed a gradual elevation with time. In tissue transplantation, and especially in free flaps, blood supply to the tissue depends on 1 or 2 small arteries. With time, vascularization is slowly established between the graft bed and the flap. The gradual increase in the postoperative blood glucose level in flaps seems to reflect this hemodynamic change: The blood supply to the flap may be insufficient soon after the operation, but it improves with time. Except for the initial glucose fall in flaps similar glucose profiles and glucose concentrations were recorded in flap and finger tip. The initial fall was not statistically significant.

BGM also cannot be used in patient undergone buried tissue transfer. It is also uncertain if BGM for flap monitoring can be used in diabetic patients, since the blood glucose level often fluctuates at both higher and lower values which are more than that in non-diabetic persons. Therefore, it may be necessary to modify the blood glucose values obtained from diabetic patients, and further studies on this issue are needed. For BGM, the flap needs to be traumatized using a needle. Although the flap can be damaged by this method, especially in cases where multiple BGMs are necessary in a small flap, no flaps were lost due to skin puncture by this method in our experience. In addition, this method

is safe because the depth of the puncture was set to 1.8 mm, which corresponds to the depth of the dermal layer in the back or abdomen.

The BGM method described here is simple and can be performed by residents, nurses, and patients themselves by using the current flap monitoring instruments. Blood flow in the flap can be determined quantitatively in cases in which blood flow is decreased as determined by the physical appearance or a pinprick test. Application of BGM to flap monitoring is particularly useful for comparing the blood flow condition with that of a few hours earlier, and the results can be easily communicated to the medical staff. BGM may also be useful for monitoring intraoral flaps, which are difficult to monitor on the basis of flap color or in tissue transfer with a small skin paddle.

Flap BGM has also got prognostic value, Flap BGM levels improving over a period of time is indicative of better flap perfusion while vice versa is true for ischemic flaps. Rate of flap glucose fall is highly sensitive for vessel occlusion. Faster the rate of fall of BGM is suggestive of rapid development of vascular thrombosis.

There are not many studies available in which the efficacy of flap monitoring by glucose measurement is being evaluated. Method of flap blood glucose monitoring is objective, easy to do and inexpensive method for flap monitoring which can be done by any medical professional and does not require any specialised setup.

Summary

Summary

- This was a 6 month prospective study to evaluate the efficacy and best cut off value of Flap glucose measurement by glucometer as a tool for post operative monitoring of pedicled flap and free tissue transfer. A total of 60 different flaps were included in study. Flap capillary glucose levels were measured by using accu check glucometer. Glucose levels of flap with necrosis and without necrosis were compared. Statistical analysis was done by ROC curve to determine the best cutoff value for the flap blood glucose monitoring.
- Mean age of patients was 41.5 years.
- Out of 60 different flaps 3 flaps had complete failure, 2 flaps had major partial necrosis and 11 flaps had minor partial necrosis. .
- The mean sugar value for survival and non survival group it was 109 mg/dl and 42.5 mg/dl respectively
- To detect flap ischemia a cut-off value of 61 mg/dl was determined for the flap BGM, at which the sensitivity and specificity were 93% and 80%.
- Flap blood glucose monitoring is an Objective, Easy to do, In-expensive, sensitive and specific test. This test can be done by any medical professional (Nurses/ Interns/ Paramedics) without need of any specialised setup.
- There were no major complications in our study due to the use of Glucometer as monitoring tool.
- BGM has been found to be valuable tool for early detection of flap ischemia and works as adjuvant to routine clinical flap monitoring.

Conclusion

Conclusion

- Flap capillary glucose levels less than 61 mg/dl is suggestive of ischemia of flap with sensitivity and specificity of 91% and 80 % respectively.
- Allows early detection of vascular compromise.
- Has prognostic value
- Define line of demarcation in partial necrosis

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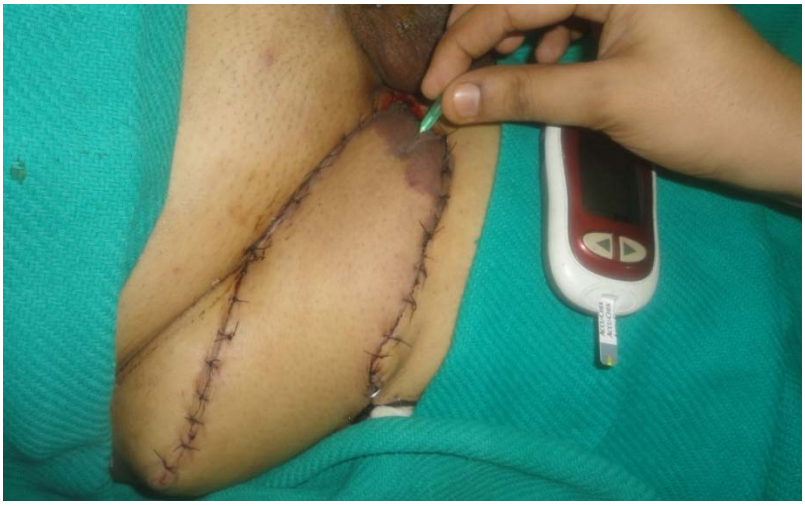
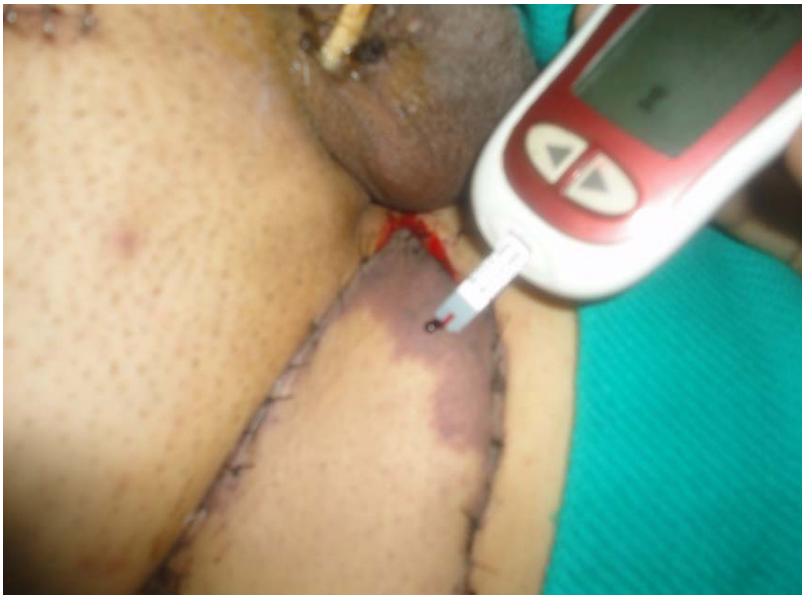
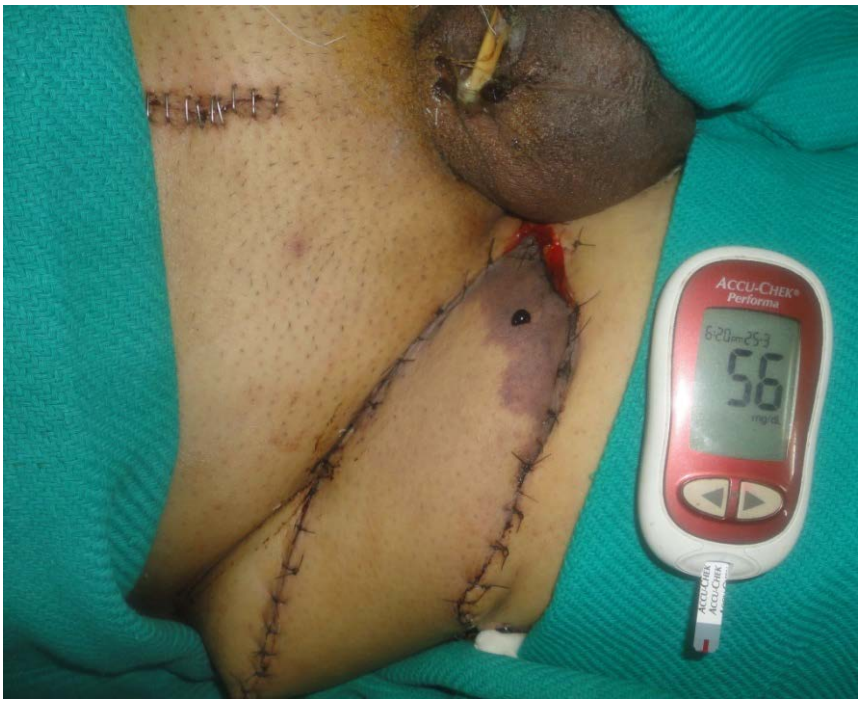
Clinical Photograph



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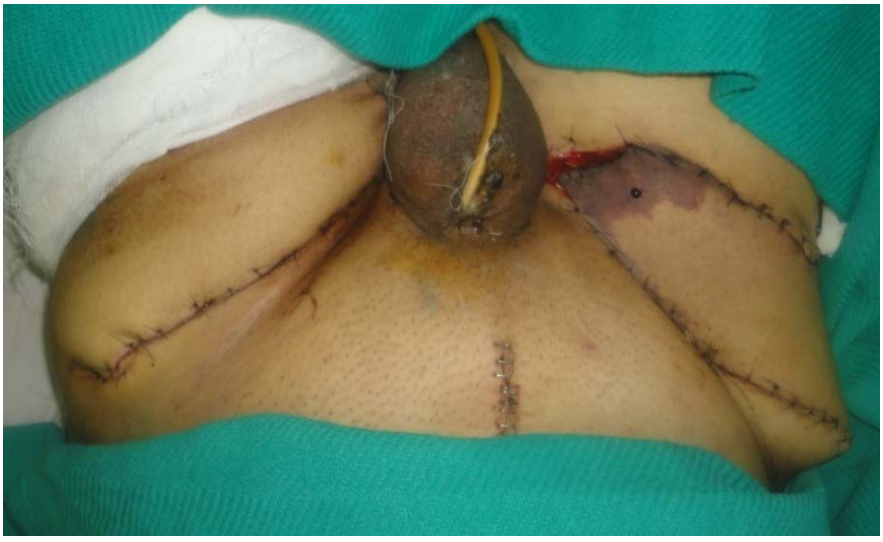
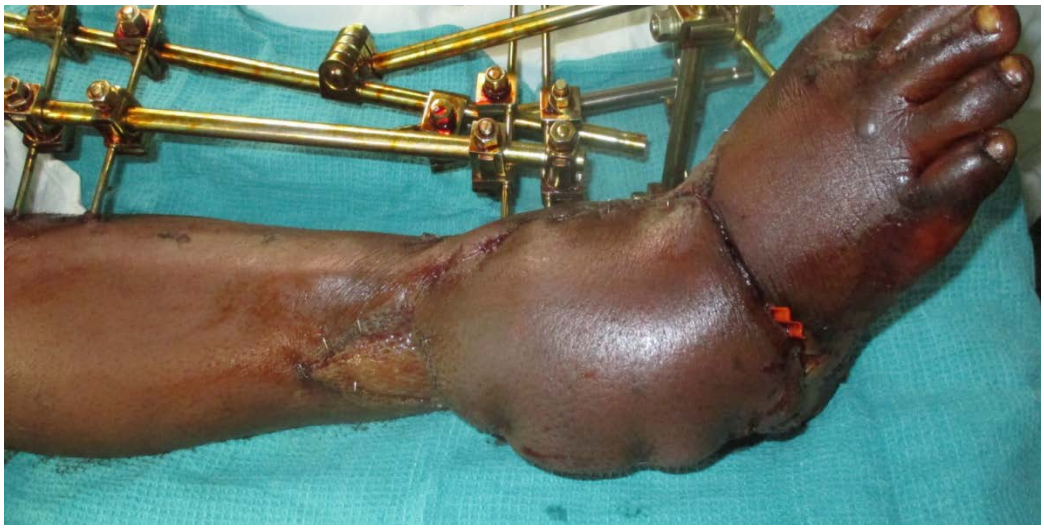
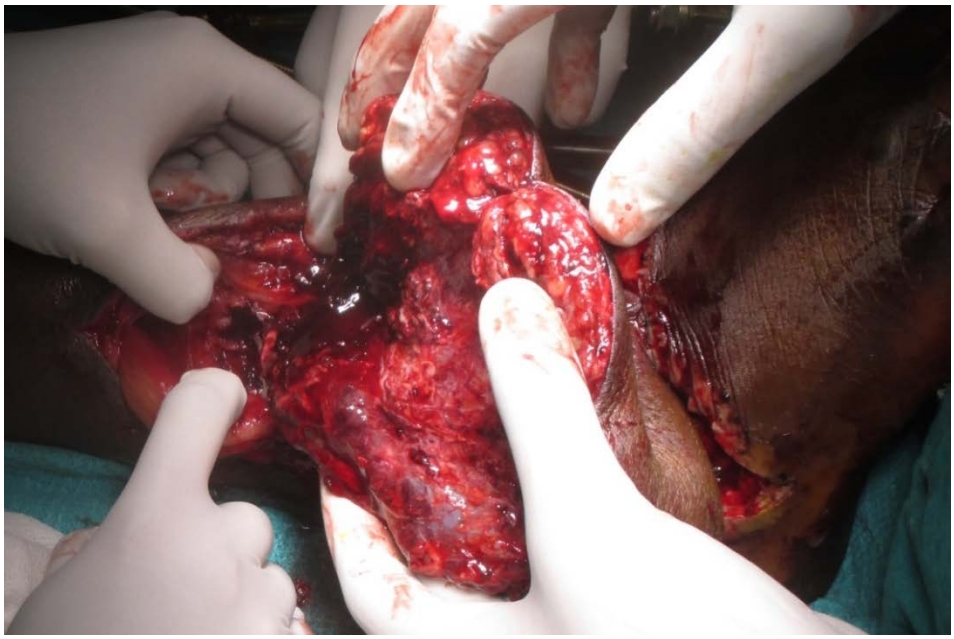




Ischemic and congested Flap



Thrombosed blood vessels in an ischemic flap

Annexure1: Proforma and consent form

Annexure 1: Proforma and consent form

Proforma

1. Name
2. Age
3. Occupation
4. HOSPITAL NUMBER
5. Diagnosis
6. Hypertension
7. Diabetes
8. Smoking
9. Co morbid condition
10. Date of surgery
11. Type of flap
12. Flap monitoring chart

Flap Monitoring Chart	Name		Hospital number
	Age	Sex	Operation date-
	Flap Location		
	Flap type		

Post OP day																									
Date																									
Time																									
COLOR	White	1																							
		2																							
		3																							
		4																							
		5																							
	pink	6																							
		7																							
		8																							
	purple	9																							
	black	10																							
capilliary refill	No refill																								
	<3 sec																								
	>3 sec																								
Texture	soft																								
	Spongy																								
	Firm																								
Temperature	cold																								
	Body temp																								
	warm																								
Doppler signal	good																								
	medium																								
	weak																								
Cappila-ry Blood glucose levels																									

CONSENT FORM

Patient information sheet

Dear patient,

My name is Dr Mukesh Kumar Sharma and I am senior registrar in department of plastic surgery. As part of my training, I am conducting a study about post operative flap monitoring by using glucometer. This study aims to provide flap glucose measurement as rapid inexpensive easy cost effective and objective method of post operative flap monitoring. At CMC hospital Vellore, All patients undergoing flap surgery in department of plastic surgery will be assessed post operatively up to 5th post operative day. Following surgery monitoring of flap will be done by clinical methods (skin paddle color, temperature, skin reperfusion time, and bleeding test with a prick) and flap capillary glucose measurement. Test will be done by pricking flap skin and measuring blood glucose by gluco-meter. Pricking of flap is not painful as flap does not have sensations. The test will be done post-operatively, hourly for first 6 hours and 6^{th} hourly thereafter for five days. Data will be analysed to know whether flap glucose measurement is a effective method of post operative flap monitoring so that early intervention can be done to salvage the flaps which are failing.

Your participation in this study is purely voluntary and if you wish at any time weather you participate of not will not affect your personal life and you may choose whether you would like to participate in this study or not. Please note that it is your right to withdraw from this study if you wish any time. You will notice that all information gathered is strictly confidential and will be used for research purpose only.

What is this study about?

To demonstrate the efficacy of capillary glucose measurement for post-operative flap monitoring.

Does participating in the study alter the treatment of the patient?

No. The patient shall be given the same treatment as planned irrespective of your decision to agree or disagree to participate in the study.

Does glucose measurement of flap by glucometer have any side effects?

No, it does not have any complication but rarely may have bleeding from the wound.

What procedure will be done if I consent for the study?

On consenting your flap will be monitored with **glucose** measurement of flap by glucometer

I have any pain or discomfort due to the procedure?

- No

Will I get compensation if I suffer damage due to the study?

- You are not likely to have any damage because of the study. But in the event of such damage, you will receive free treatment for the damages suffered by the hospital. However, no monetary compensation shall be given.

What do I have to do?

- You are asked to read this consent form in detail, clarify your doubts if any and sign at the end of the form if you decide to participate in the study

What will I have to do if I participate in the study?

- You will have to agree to be examined and ask for you to cooperate while test is done.

Can I say NO to the study?

- Your participation in the study is completely voluntary and you can choose to either enter the study or not to. Your decision will not alter your treatment in the hospital

Will my treatment details be kept confidential?

- Your personal and medical records will be kept confidential and shall be used only for academic and research purposes and may be presented or published in academic circles. However, you will not be identified personally

Can I withdraw from the study once I consent?

- Yes. You can opt out of the study if you want. However, your medical records shall be available for the academic review even if you discontinue the participation

Can my participation in the study be cancelled by the investigators?

- Yes. Your participation in the study can be rejected or cancelled without your permission or information at any stage during the study period if the investigators wish so for any reason.

If you have any more queries, please contact Dr. Mukesh Kumar Sharma PHONE: 04162282017

CELL PHONE: 91-9751831963

Informed Consent form to participate in a research study

Study Title: Prospective analysis of flap perfusion by measuring Capillary Glucose levels in pedicled flap and free tissue transfer.

Study Number:

Subject's Initials: _____ **Subject's Name**: _____

Date of Birth / Age: _____

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my participation in the study is voluntary and that I am

free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]

(iii) I understand that the Sponsor of the clinical trial, others working on the Sponsor's behalf, the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s) [ ]

(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable Representative:_____

Date: _____/_____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: _____/_____/_____

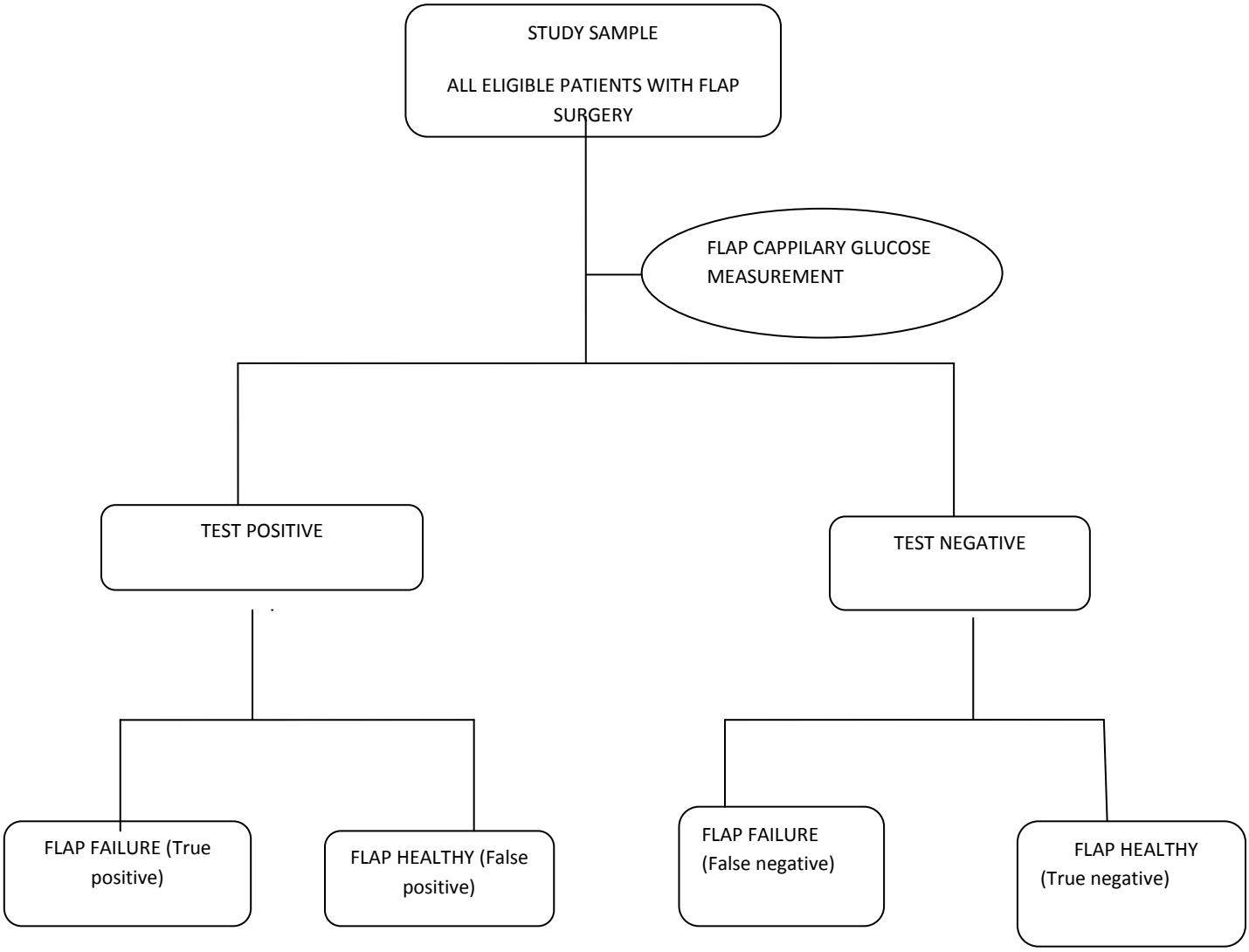
Study Investigator's Name: _____

Signature of the Witness: _____

Date:_____/_____/_____

Name of the Witness: _____

Algorithm of the study



S. No.	HOSP No.	AGE	SEX	Comorbidities	Diagnosis	Cause	FLAP	Typer of flap	Complication	RESULT	0 HOUR	6 Hour	12 Hour	18 Hour	24 Hour	30 Hour	36 Hour	42 Hour	48 Hour	54 Hour	60 Hour	66 Hour	72 Hour	78 Hour	84 Hour	90 Hour	96 Hour	102 Hour	108 Hour	114 Hour	120 Hour
1	455975f	31	M	NIL	CRUSH INJURY RIGHT ANKLE	Trauma	left anterolateral thigh microvascular flap	Free flap	Nil	1	154	138	148	144	118	124	96	109	122	116	122	130	131	132	119	127	140	101	136	127	133
2	345524F	71	M	NIL	Squamous cell carcinoma penis	Malignancy	Anterolateral Thigh Flap	Pedicled axial flap	Nil	1	82	112	111	119	101	132	127	121	129	132	122	117	109	94	134	149	126	109	132	111	131
3	435660F	52	M	NIL	SCC penis	Malignancy	TFL flap	Pedicled axial flap	Nil	1	136	111	123	105	122	117	113	126	129	112	129	104	102	118	122	120	117	139	124	121	134
4	457794F	44	M	Diabetic	SOFT TISSUE DEFECT RIGHT CHEEK POST OP RIGHT MAXILLECTOMY	Malignancy	LEFT PARAMEDIAN FOREHEAD FLAP	Pedicled axial flap	Nil	1	134	155	124	111	136	124	144	130	92	116	121	101	118	172	130	132	122	119	127	155	173
5	458560F	33	m	NIL	DEGLOVED RIGHT ELBOW	Trauma	Inferiorly based abdominal flap	Random flap	Minor Partial Necrosis	2	58	27	36	12	21	0	0															
6	474214F	37	M	NIL	ELECTRICAL BURNS	Burn	groin flap cover for soft tissue defect of wrist	Pedicled axial flap	Nil	1	112	132	144	122	156	117	147	137	129	117	152	97	112	106	129	137	122	138	112	141	121
7	461900F	21	F	NIL	SCARRING AND STIFFNESS RIGHT ELBOW	Trauma	Abdominal flap cove	Random flap	Minor Partial Necrosis	2	18	22	12	32	0	0	0															
8	353927F	51	F	Diabetic	CARCINOMA LEFT BREAST	Malignancy	LATISSMUS DORSI MUSCLE FLAP	Pedicled axial flap	Nil	1	224	255	105	166	172	136	196	226	217	196	117	144	156	149	188	193	228	170	122	118	123
9	468319F	34	M	NIL	ULCER PROXIMAL THIRD OF RIGHT LEG	Trauma	local transposition flap	Random flap	Nil	1	94	42	79	114	96	112	80	74	96	114	132	140	122	137	101	122	101	99	112	121	118
10	467764F	69	M	NIL	Carcinoma penis	Malignancy	ALT flap cover	Pedicled axial flap	Nil	1	122	116	110	84	144	128	184	166	146	112	117	134	142	152	177	117	158	144	132	127	112

11	467764F	69	M	NIL	Carcinoma penis	Malignancy	ALT flap cover	Pedicled axial flap	Minor Partial Necrosis	2	0	0	0																	
12	497783F	31	F	NIL	SCALP DEFECT	Trauma	Local transposition flap	Random flap	Nil	1	88	136	128	154	137	146	122	152	157	146	155	142	155	112	152	110	122	127	121	101	132
13	103226F	32	M	NIL	POST BURN CONTRACTURE BILATERAL AXILLAE.	Burn	Propellar flap coverge for left axillary defect	Pedicled axial flap	Nil	1	126	129	106	144	110	132	146	137	128	118	137	129	117	105	113	129	154	128	122	131	118
14	370642F	43	M	NIL	CARCINOMA BREAST - RIGHT BREAST	Malignancy	LD FLAP RECONSTRUCTION	Pedicled axial flap	Nil	1	136	148	155	122	112	126	104	136	166	157	154	139	152	162	128	144	133	121	12	181	112
15	494231f	55	f	NIL	EXPOSED IMPLANT RIGHT ELBOW	Trauma	right laterally based pedicled abdomen flap cover	Pedicled axial flap	Nil	1	116	144	139	164	136	137	117	143	156	144	128	137	119	123	146	152	147	137	128	127	131
16	492373f	16	M	NIL	mandible defect	Malignancy	free fibula flap	Free flap	Nil	1	88	110	127	134	145	122	116	101	147	119	129	146	145	139	127	137	122	147	129	118	110
17	594037d	33	M	NIL	POST TRAUMATIC SOFT TISSUE LOSS LEFT FOOT AND LOWER 1/3RD OF LEG	Trauma	Left Free Latissimus dorsii flap	Free flap	Nil	1	86	118	147	134	152	117	95	122	107	126	137	142	128	117	129	143	107	133	125	131	
18	611562F	15	M	NIL	POST TRAUMLEFT ELBOW DEFECT	Trauma	Abdominal flap cover	Pedicled axial flap	Nil	1	92	122	118	104	126	129	137	116	127	134	101	107	132	127	126	122	119	126			

19	635470F	25	M	NIL	POST ELECTRICAL BURN SOFT TISSUE DEFECT LEFT PARIETO-OCCIPITAL REGION WITH EXPOSED CALVARIUM	Trauma	local transposition flap	Random flap	Nil	1	88	116	122	110	122	116	129	123	108	117	111	137	117	107	96	99	133				
20	611851F	49	M	NIL	LEFT LEG DISTAL SOFT TISSUE DEFECT WITH EXPOSED IMPLANT	Trauma	Cross leg flap	Random flap	Minor Partial Necrosis	2	84	69	52	37	38	26	29	16	0	0	0										
21	644937F	36	F	NIL	OSTEOMYELITIC RIGHT FRONTAL BONE FLAP	Post Surgical	rotation skin flap based on right post auricular artery and occipital artery	Pedicled axial flap	Nil	1	116	113	101	97	112	79	89	94	97	113	107	113	122	131	117	107	129	141	112	121
22	611851F	49	m	NIL	LEFT LEG DISTAL SOFT TISSUE DEFECT WITH EXPOSED IMPLANT	Trauma	local transposition Flap	Random flap	Major Partial Necrosis	2	87	48	63	29	48	36	39	41	32	30	34	41	42	26	21	0	0	0		
23	641878F	59	M	NIL	Carcinoma penis	Malignancy	TFL flap	Pedicled axial flap	Nil	1	59	88	126	116	129	127	137	143	129	109	112	119	137	143	131	152	112	126	133		
24	641878F	59	M	NIL	Carcinoma penis	Malignancy	ALT flap cover	Pedicled axial flap	Nil	1	64	67	97	114	122	126	137	141	127	109	117	122	132	141	131	119	117		132		
25	657672F	35	M	NIL	LEFT LEG DEFECT	Trauma	Cross leg flap	Random flap	Nil	1	102	84	115	116	112	126	116	97	117	92	104	107	113	87	93	99	119				

26	601350F	35	M	NIL	LOWER 1/3RD - NOSE DEFECT WITH LEFT CLAW HAND	Leprosy	Forehead Flap cover	Pedicled axial flap	Nil	1	63	88	112	90	110	117	113	114	107	93	112	97	99	129	133	101	97	119	116
27	639778F	39	M	NIL	POST TRAUMATIC DEFECT OVER RIGHT PROXIMAL TIBIA AND RIGHT FOOT DORSUM	Trauma	Free Latissimus dorsi Muscle flap cover for the right Foot	Free flap	Nil	1	69	67	99	112	118	124	136	143	143	172	129	142	127	119	129	113	127	122	
28	664885F	30	M	NIL	POST TRAUMATIC AVULSION INJURY OF LEFT SIDE OF THE FACE AND LEFT INFRACLAVICULAR FOSSA	Trauma	pectoralis Major muscle transposition flap	Pedicled axial flap	Nil	1	112	122	154	159	112	124	110	129	116	124	116	136	128	97	117	144	113	119	108
29	671495F	5	F	NIL	RIGHT FOOT SOFT TISSUE LOSS	Trauma	Right sural artery flap	Pedicled axial flap	Minor Partial Necrosis	2	18	22	12	27	34	15	0	0											
30	639778F	39	M	NIL	POST TRAUMATIC DEFECT OVER RIGHT PROXIMAL TIBIA AND RIGHT FOOT DORSUM	Trauma	Right Lateral gastrocnemius Flap cover	Pedicled axial flap	Nil	1	112	119	127	118	129	132	142	129	119	129	132	108	118	129	122	123	141	129	122
31	678734f	52	M	NIL	POST TRAUMATIC EXPOSED LEFT TENDOACHILLIS	Trauma	REVERSE SURAL ARTERY FLAP	Pedicled axial flap	Major Partial Necrosis	2	69	47	49	53	44	39	19	16	0	0	0								

32	434442F	48	M	NIL	SCC PENIS	Malignancy	TFL Flap	Pedicled axial flap	Nil	1	57	72	119	134	142	117	87	92	113	129	130	127	108	112	122	134	112	129				
33	434442F	48	M	NIL	SCC penis	Malignancy	TFL Flap	Pedicled axial flap	Nil	1	88	104	112	134	141	117	87	93	117	122	130	127	108	113	127	137	113	127				
34	671623F	45	M	NIL	CRUSH INJURY RIGHT UPPER LIMB	Trauma	RIGHT LATISSIMUS DORSI FLAP	Pedicled axial flap	Nil	1	101	117	122	127	97	94	87	132	132	128	117	116	72	93	97	113	128	129	134	121		
35	485748F	19	M	NIL	RIGHT DISTAL FEMUR FRACTURE WITH IMPLANT INSITU	Trauma	medial gastrocnemius flap cover	Pedicled axial flap	Nil	1	72	94	97	110	84	87	98	112	126	143	127	122	127	117	128	107	108	122	122		
36	071171C	59	M	NIL	CHRONIC NON HEALING ULCER RIGHT INGUINAL REGION	Malignancy	TFL flap cover	Pedicled axial flap	Nil	1	93	126	122	123	107	124	129	127	127	134	137	128	137	128	143	121	137	128	110	126	107	133
37	338364F	27	F	NIL	POST BURN CONTRACTURE BILATERAL HAND AND WRIST	Burn	periumbilical based abdominal flap	Random flap	Nil	1	117	127	144	129	118	127	101	97	98	88	113	87	129	139	129	130	137	136	124			
38	682262F	51	F	NIL	SOFT TISSUE DEFECT RIGHT ELBOW	Trauma	abdominal Flap	Random flap	Minor Partial Necrosis	1	84	62	0	57	47	77	92	93	87	97	93	89	112	122	104	112	123	133	129	117		
39	675844F	45	F	NIL	DEGLOVING INJURY RIGHT FOOT WITH FRACTURED MEDIAL MALLEOLUS	Trauma	Peroneus brevis flap	Pedicled axial flap	Minor Partial Necrosis	1	88	84	86	76	89	97	86	102	122	97	91	86	105	113	110	131	111					
40	345524F	70	M	NIL	SCC PENIS	Malignancy	TFL flap	Pedicled axial flap	Minor Partial Necrosis	2	54	42	47	49	36	34	27	20	18	0	0	0										
41	345524F	70	M	NIL	SCC PENIS	Malignancy	ALT flap cover	Pedicled axial flap	Minor Partial Necrosis	2	56	61	73	44	37	18	0	0	0													

42	666022F	45	F	NIL	SCALP SOFT TISSUE DEFECT WITH EXPOSED IMPLANT LEFT FRONTAL REGION	Trauma		Pedicled axial flap	Minor Partial Necrosis	2	72	76	62	46	44	47	32	36	31	22	0	0	0						
43	071171C	59	M	NIL	CHRONIC NON HEALING ULCER RIGHT INGUINAL REGION	Malignancy	TFL flap	Pedicled axial flap	Minor Partial Necrosis	2	88	43	46	32	37	18	16	0	0	0									
44	042093C	30	F	NIL	RIGHT LEG WITH OPEN TYPE 3B RIGHT LEG BOTH BONE FRACTURE	Trauma	right Ponten flap cover for middle 1/3 exposed tibial defect	Pedicled axial flap	Major Partial Necrosis	2	56	48	44	29	36	32	38	27	16	19	0	0	0						
45	726484F	5	M	NIL	POST TRAUMATIC DEGLOVING INJURY LEFT FOOT	Trauma	left peroneus brevis muscle flap	Pedicled axial flap	Nil	1	88	112	134	129	144	128	132	144	119	128	118	133	127	132	156	122	118	127
46	475480F	16	F	NIL	CEMENTO-OSSIFYING TUMOR OF LEFT JAW	Malignancy	vascularised free osteocutaneous fibula flap	Free flap	Nil	1	34	29	26	37	44	75	66	43	69	76									
47	697458F	22	F	NIL	LUMBAR MYELOMENINGOCELE	benign disease	Rotation flap	Random flap	Nil	1	112	117	129	104	134	156	147	129	143	134	129	133	129	122	137	119	115	125

48	720127F	33	M	NIL	Post traumaSOFT TISSUE DEFECT RIGHT LOWER LIMB WITH EXPOSED TIBIA	Trauma	LEFT CROSS LEG FLAP	Random flap	Nil	1	98	87	104	128	132	129	122	127	126	119	139	123	141	123	166	121	131	129	
49	435660F	52	M	NIL	SCC penis	Malignancy	TFL flap	Pedicled axial flap	Nil	1	122	119	123	109	104	118	131	127	113	127	119	127	124	137	132	119	105	115	
50	229014F	49	F	NIL	MALIGNANT MELANOMA LEFT HEEL	Malignancy	Reverse sural artery flap	Pedicled axial flap	Nil	2	83	72	52	54	56	37	34	42	29	11	16	0	0	0					
51	214344F	45	M	NIL	Squamous cell carcinoma	Malignancy	TFL flap	Pedicled axial flap	Nil	1	104	126	131	123	122	131	126	129	131	117	112	110	116	123	117	129	132	127	118
52	269626F	31	M	NIL	RAW AREA OVER THE RIGHT ANKLE JOINT	Trauma	Free Gracilis flap right leg	Free flap	Complete loss	2	33	18	29	21	0	0	0												
53	272767F	22	M	NIL	POST BURN CONTRACTURE RIGHT HAND .	Burn	reverse radial forearm pedicled flap	Pedicled axial flap	Nil	1	98	117	126	137	129	122	126	119	108	132	122	105	117	126	131	129	133	131	119
54	301849F	62	F	NIL	BASAL CELL CARCINOMA-LEFT MEDIAL CANTHUS	Malignancy	TEMPORAL MUSCLE AND FASCIA FLAP + CHEEK ADVANCEMENT FLAP + CONTRALATERAL GLABELLAR FLAP COVER +SKIN GRAFTING	Random flap	Nil	1	117	106	127	112	116	117	119	121	131	142	137	129	119	131	110	128	131	110	

55	300732F	28	F	NIL	MALIGNANT PHYLLODES TUMOUR - LEFT BREAST	Malignancy	LATISMUS DORSI FLAP	Pedicled axial flap	Nil	1	87	112	127	112	129	131	129	131	129	131	144	127	109	129	131	128	122			
56	322482F	56	M	NIL	CRUSH INJURY LEFT FOOT	Trauma	Reverse sural artery flap	Pedicled axial flap	Major Partial Necrosis	2	71	43	41	32	37	31	36	21	20	0	0	0							
57	299612F	20	M	NIL	25% ELECTRICAL BURNS INJURY	Burn	calf fasciocutaneous flap	Pedicled axial flap	Nil	1	82	112	116	129	132	116	111	121	112	131	126	129	108	127	132	122	129			
58	612296C	40	M	NIL	LEFT PALATAL DEFECT FOR MUCOEPIDEMOID CARCINOMA MAXILLA	Malignancy	FREE RADIAL FOREARM FLAP (LEFT FOREARM DONOR SITE)	Free flap	Complete loss	2	47	42	27	24	16	13	0	0	0										
59	751045f	32	M	NIL	SOFT TISSUE DEFECT RIGHT FOOT.	Trauma	free Anterolateral thigh Flap cover	Free flap	complete loss	2	61	34	33	39	21	0	0	0											
60	419203f		M	NIL	RIGHT LEG -CHRONIC OSTEOMYELITIS OF MIDDLE 1/3 OF TIBIA	Trauma	Free Latissimus dorsi Muscle flap cover for the right Foot	Free flap	Nil	1	93	111	129	84	132	124	120	116	121	109	133	128	110	97	127	122	110	131	121	122