Applications of Angiosome Classification Model for Monitoring Disease Progression in the Diabetic Feet

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Abstract
"Every 20 seconds there is a diabetes related amputation somewhere in the world". Diabetes affects 382 million people in the world today and by 2035, at least 592 million people will have diabetes- approximately 10% of the world's adult population. One of the most sinister complications of diabetes is peripheral neuropathy, where patients loose the gift of pain in their feet. Presently, clinicians assess circulation, neuropathy, and plantar pressures to identify the risk of foot ulceration that when get infected lead to amputations. The key common factor that appears to be present both in dysfunctional healing and in predicting breakdown may be inflammation. Inflammation is a central unifying concept of medicine spanning across the spectrum of pathologies from a simple bruise to cancer. For a diabetic wound, uncontrolled inflammation produces staggering impact for the patients as well as the healthcare system. Currently, there are no objective means of measuring wound inflammation and surprisingly the status quo is 'measurements of temperatures using back of the hand'. This paper presents a conceptual methodology for classification of thermograms based on the angiosomes of the feet.

1. DIABETIC WOUNDS

"Every 20 seconds there is a diabetes related amputation somewhere in the world". Diabetes affects 382 million people in the world today and by 2035, at least 592 million people will have diabetes- approximately 10% of the world's adult population. Half of the people with diabetes don't know that they have it.[1] One of the most sinister complications of diabetes is peripheral neuropathy, where patients loose the gift of pain in their feet. Almost, 60-70% of those with diabetes will develop peripheral neuropathy, or lose sensation in their feet. This condition increases the risk of skin breakdown resulting in wounds or ulcers. Up to 25% of those with diabetes will develop a foot ulcer in their lifetime.[1] Almost 50% of these wounds become infected, 20% of which result in lower extremity amputations. After a major amputation, 50% of people will have their other limb amputated within 2 years. [2, 3]

Identifying areas of injury by the presence of inflammation would allow patients or health care providers to take action to decrease the inflammation before a wound develops.[4, 5] Personal dermal thermometers already exist and have been shown to be clinically useful in reducing the rates of re-ulcerations.[6-8] However, significant involvement of microvascular disease predisposes skin tissue to ulceration and therefore, novel techniques are needed to differentiate between vascular and cellular indicators of metabolic status This may be deemed useful better clinical diagnosis especially in patients with a history of ulceration and/or amputations.

1.1. Inflammation

Presently, clinicians assess circulation, neuropathy, and plantar pressures to identify the risk of foot ulceration.[9] Several studies have suggested prevention of foot ulcers by identifying individuals at high risk and treating for lower extremity complications. [10-12] Current assessment of severity of diabetic foot disease is subjective The key common factor that appears to be present both in dysfunctional healing and in predicting breakdown may be inflammation. Inflammation is a central unifying concept of medicine spanning across the spectrum of pathologies from a simple bruise to cancer. For a diabetic wound, uncontrolled inflammation produces staggering impact for the patients as well as the healthcare system. Currently, there are no objective means of measuring wound inflammation and surprisingly the status quo is 'measurements of temperatures using back of the hand'.

Thermography provides non-invasive imaging of inflammation and can be used to objectively assess changes on the skin surface to diagnose pathological disease states.[13-17]

1.2. Angiosomes

Nagase et al. 2011 developed a novel classification system for planter thermal patterns based upon the angiosomes of the foot. The concept of angiosomes was defined in 1987 by Ian Taylor as separate three-dimensional anatomic units of tissue each fed by a source artery. The foot and ankle are comprised of six distinct angiosomes. Four angiosomes supply the plantar foot: the medial plantar artery (MPA) angiosome, lateral plantar artery (LPA) angiosome, medial calcaneal artery (MCA) angiosome, and lateral calcaneal artery (LCA) angiosome. Adjacent angiosomes are connected by small vessels known as choke vessels that dilate when the flow from a direct source artery is diminished or blocked. It can take days or weeks for the choke vessels to completely dilate.

There are five possible patterns developed to illustrate the distal region (Figure 1). Type I shows the 'bilateral butterfly pattern' that was discovered in a previous study to be the most common pattern in normal subjects where the highest temperatures are located in the medial arch. Type II represents both the MPA and LPA undamaged. Type III represents when the MPA is compromised. Type IV represents when the LPA is compromised. Type V represents when both the MPA and LPA are compromised. The compromised angiosomes are supplied by choke vessels and therefore will have lower temperature readings than angiosomes that are intact.

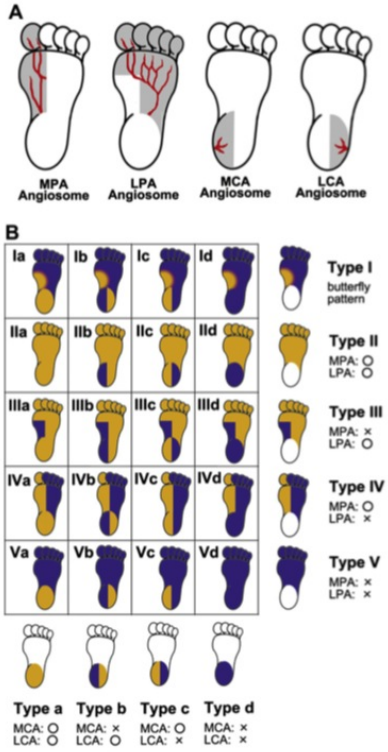


Figure 1: Conceptual model of plantar angiosomes (Courtesy: Journal of Plastic, Reconstructive & Aesthetic Surgery, Nagase et al. (2011) [18]).

This paper presents a conceptual methodology for classification of thermograms based on the angiosomes of the feet.

2. METHODS

Upon approval from the Institutional Review Board for this study, we enrolled 12 subjects - 6-Diabetics with Peripheral Neuropathy (DMPN) & 6 controls. All subjects were recruited from the Southern Arizona Limb Salvage Alliance (SALSA) at the University of Arizona's University Medical Center in Tucson. There were 3 study related visits – baseline, 6-week and 12-week. During the follow up visits we measured any potential signs of skin breakdown or ulcer. An ulcer is defined as the full thickness loss of epidermis and dermis layers including deeper structures. Patients were excluded from the study if they had any open ulcers or open amputation sites, active Charcot arthopathy, hammertoe, active foot infection, dementia, impaired cognitive function, history of alcohol or drug abuse within one (1) year of the study.

As part of the study protocol, subjects were tested for neuropathy using 5.07 Semmes Weinstein monofilament and vibratory perception threshold (VPT). A VPT score of >25 was considered as presence of neuropathy. All subjects were clinically examined including visual assessment for the presence of callus, fissures, or dryness. A repetitive stress test was performed during each clinical visit. For this test, subjects were allowed to acclimatize with ambient conditions for 20 minutes after visual examination was performed. The room temperature and humidity will be maintained at 24^0C and less than 50% respectively with air conditioning. Then the foot temperature was measured using a handheld infrared scanner. After the first scan, patients were instructed to walk for 20 minutes and upon return their feet were again imaged using the infrared scanner. This measurement assessed the physiological response to stress. Subsequently, we waited for 10 minutes to acquire another thermal image to assess post stress recovery.

Foot temperature were recorded for both right and left limbs at 5 sites with highest risk for ulceration. Nagase et al. conceptual model was then used to record the type of angiosome at each condition[18].

3. RESULTS

This was a cross-sectional study with 12 study subjects (6 DMPN and 6 Healthy Volunteers). For each study visit, each plantar thermographic image was allocated to the 20

different categories, (Figure 1), by one of the co-authors. To avoid observation bias, this allocation was further confirmed by an additional co-author. When the allocations differed among the investigators, the images were reviewed again by both investigators to make a final decision. If the images did not correspond to any of the 20 categories, they were designated as 'atypical'. The classification framework was directly applied from the prior works of Nagase et al (2011). [18] However, due to a small sample size we did not identify any atypical categories. Nagase et al. (2011) have reported 15% atypical feet (control group) and 12.8% atypical feet in patient group, in their study of 129 healthy controls and 32 diabetic patients.

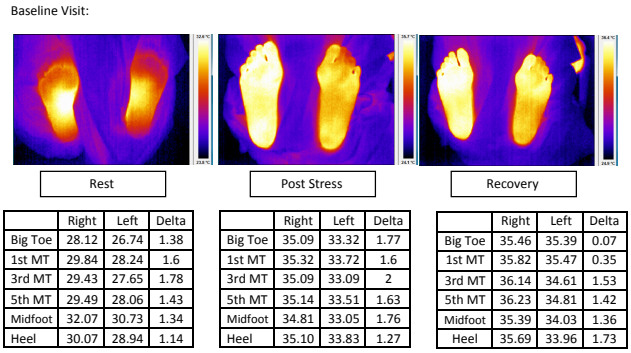
Tables 1 & 2 summarize the angiosomes classification for both groups respectively. Additionally, Figure 2 illustrates the delta temperatures at 6 high risk sites for a healthy volunteer. Similar computations were carried out for all subjects and averaged to provide a mean delta temperature at each of the high risk site (Table 3).

Healthy		Rest		Post Stress		Recovery	
		Right	Left	Right	Left	Right	Left
1	Baseline	IVd	Id	IIa	IIa	IIa	IIa
	6-Week	Vd	Vd	IIa	IIa	IIb	IId
	12-Week	IVa	Id	IIa	IIa	IVa	IVd
2	Baseline	Id	Vd	IIa	IIa	IIa	IIa
	6-Week	Vd	Vd	IIa	IIa	IIa	IIa
	12-Week	IIa	IIa	IIa	IIb	IIa	IIa
3	Baseline	Id	Id	Id	Id	Id	Id
	6-Week	Id	Id	Id	Id	Id	Id
	12-Week	IId	Id	IId	IId	Id	Id
4	Baseline	Id	Id	IVc	Ia	Vd	Vd
	6-Week	Id	Id	IVa	Vc	Id	Id
	12-Week	Vd	Id	Vd	Vd	Vd	Id
5	Baseline	IId	Id	IId	IIId	IId	IIId
	6-Week	IIId	IIId	IIa	IIa	IIId	IIId
	12-Week	IId	Id	IIId	Vd	IIId	IIId
6	Baseline	Vd	Vd	Vd	IVd	Vd	Vd
	6-Week	Id	Ia	IId	IIa	IVd	IVa
	12-Week	Id	Ia	Id	Vd	Id	Ia

Table 1: Summary of angiosomes classification for 6 Healthy Volunteers.

DMPN		Rest		Post Stress		Recovery	
		Right	Left	Right	Left	Right	Left
1	Baseline	Ib	Id	IIIa	IIIa	IIIb	IIb
	6-Week	IIa	IIa	IIa	IIa	IIa	IIa
	12-Week	Id	Id	IIIa	IIa	Vd	Vd
2	Baseline	IIa	IIa	IIa	IIa	IIa	IIa
	6-Week	n/a	n/a	n/a	n/a	n/a	n/a
	12-Week	n/a	n/a	n/a	n/a	n/a	n/a
3	Baseline	IVa	IVa	Va	IVa	Vc	IVa
	6-Week	IVa	IIa	Vc	IVa	Vc	IVa
	12-Week	Vc	IIa	Vc	Vc	Vc	Vc
4	Baseline	IIId	IIa	Vd	IIa	Vd	IIId
	6-Week	IIIa	n/a	IIIa	n/a	IIa	n/a
	12-Week	Vd	Vd	Vd	Vd	Vd	Vd
5	Baseline	IIa	IIa	IIa	IIa	IIa	IIa
	6-Week	IIa	IIa	IIa	IIa	IIc	IIb
	12-Week	IIa	IIa	IIa	IIa	IIc	IIb
6	Baseline	n/a	IVa	n/a	IIa	n/a	IIa
	6-Week	n/a	IIa	n/a	IIa	n/a	Vd
	12-Week	n/a	Id	n/a	IIId	n/a	Vd

Table 2: Summary of angiosomes classification for 6 DMPN Subjects.



	Right	Left	Delta
Big Toe	28.12	26.74	1.38
1st MT	29.84	28.24	1.6
3rd MT	29.43	27.65	1.78
5th MT	29.49	28.06	1.43
Midfoot	32.07	30.73	1.34
Heel	30.07	28.94	1.14

	Right	Left	Delta
Big Toe	35.09	33.32	1.77
1st MT	35.32	33.72	1.6
3rd MT	35.09	33.09	2
5th MT	35.14	33.51	1.63
Midfoot	34.81	33.05	1.76
Heel	35.10	33.83	1.27

	Right	Left	Delta
Big Toe	35.46	35.39	0.07
1st MT	35.82	35.47	0.35
3rd MT	36.14	34.61	1.53
5th MT	36.23	34.81	1.42
Midfoot	35.39	34.03	1.36
Heel	35.69	33.96	1.73

Figure 2: Delta Temperatures at high risk sites.

	Rest					
	Great Toe	1st MTH	3rd MTH	5th MTH	Mid Foot	Heel
Healthy	1.245	0.91	1.05	0.96	0.505	0.48
Neuropathy	0.775	0.61	0.465	0.3	0.445	0.55
	Post Stress					
Healthy	0.825	0.85	0.815	0.915	0.715	0.41
Neuropathy	1.31	0.945	0.855	0.215	0.445	0.595
	Recovery					
Healthy	1.135	0.915	1.29	1.09	0.625	0.715
Neuropathy	0.985	1.11	0.82	0.31	0.55	0.455

Table 3: Summary of delta temperatures for all subjects.

4. DISCUSSION

This study provides a basis for classifying thermographic images of the feet per the novel classification suggested by Nagase et al (2011). [18] Use of thermography generally helps achieving a comprehensive understanding of the significance of temperature changes on the skin surface and

its association with underlying pathology. Use of thermal techniques has largely remained a research tool, however availability of quantitative tools may help clinical integration and routine assessments.

Thermography of the healthy group revealed that the Id category was the representative category in this group. Considering each limb independently, there were 36 healthy limbs scanned for rest, post stress and recovery conditions between the 3 study related visits. For the healthy group, there were 47.2%, 13.8% and 27.8% subjects representing Id classification at rest, post stress and recovery measurements respectively. Similarly, there were 5.5%, 38.9% and 22.2% subjects representing IIa classification at rest, post stress and recovery measurements respectively.

Thermography of the DMPN group revealed that the IIa category was representative category in this group. Considering each limb independently, there were 28 DMPN limbs scanned for rest, post stress and recovery conditions between the 3 study related visits. The one's marked 'n/a' were amputated and not measured during the study. For the DMPN group, there were 50%, 50% and 28.57% subjects representing IIa classification at rest, post stress and recovery measurements respectively. The IIa category was more frequent in the DMPN group than in the control group, possibly reflecting chronic temperature elevation in diabetic neuropathic feet. From the recovery standpoint, DMPN group suggests a diminished response to recovery from physical stress. This is verified by current literature and poor hyperemic response regulation in this population.[13, 19, 20] It is also of note that, 21.4%, 32.1% and 46.4% subjects representing IV or V classification at rest, post stress and recovery measurements. These two types suggest stenosis of the LPA or the more proximal artery (such as the posterior tibial artery), probably requiring routine foot care for preventing diabetic ulceration.

The low number of study participants is a major limitation of the study. Additionally, age and sex were not matched in our groups, and this may provide confounding factors for interpretation of the data. In future, we envision to study the inter-observer variability and assesss the accuracy of manually assigning images to various categories.

Another important limitation of our study is that the proposed novel classification with 20 categories may be too complicated for clinical decision making, especially due to manual classification by humans. In future, we expect to automate the identification of angiosome classification to remove any measurement bias. This could be accomplished by extending the classification into a mathematical model that allows for more elaborate quantitative representation of thermal patterns with the goal to eliminate observational bias in the current scheme.

5. CONCLSUION

Despite these limitations, we consider that thermography is a useful imaging modality in management of the diabetic foot disease. If we identify that blood supply of a particular angiosome is compromised through the proposed classification, we can pay closer attention to prevent diabetic ulcer formation in this population. Generally, the angiosome concept is quite important for planning surgical incisions, flaps and amputation level. Our investigation suggests its role in prevention of foot ulcers. Future studies will employ larger patient population to refine the classification model.

6. REFERENCES

1. Singh, N., D.G. Armstrong, and B.A. Lipsky, *Preventing foot ulcers in patients with diabetes.* Jama, 2005. **293**(2): p. 217-28.
2. Armstrong, D.G., et al., *The Impact and Outcomes of Establishing an Integrated Interdisciplinary Surgical Team To Care for The Diabetic Foot.* Diabetes/metabolism research and reviews, 2012.
3. Wu, S.C., W. Marston, and D.G. Armstrong, *Wound care: the role of advanced wound-healing technologies.* Journal of the American Podiatric Medical Association, 2010. **100**(5): p. 385-94.
4. Bharara, M., *Liquid Crystal Thermography in Neuropathic Assessment of the Diabetic Foot*, in *Academic Biomedical Engineering Research Group, School of Design, Engineering & Computing*. 2007, Bournemouth University: Bournemouth, UK.
5. Bharara, M., J.E. Cobb, and D.J. Claremont, *Thermography and thermometry in the assessment of diabetic neuropathic foot: a case for furthering the role of thermal techniques.* Int J Low Extrem Wounds, 2006. **5**(4): p. 250-60.
6. Armstrong, D.G., et al., *Skin temperature monitoring reduces the risk for diabetic foot ulceration in high-risk patients.* Am J Med, 2007. **120**(12): p. 1042-6.
7. Armstrong, D.G., et al., *Does dermal thermometry predict clinical outcome in diabetic foot infection? Analysis of data from the SIDESTEP* trial.* Int Wound J, 2006. **3**(4): p. 302-7.
8. Armstrong, D.G., *Infrared dermal thermometry: the foot and ankle stethoscope.* J Foot Ankle Surg, 1998. **37**(1): p. 75-6.

9. Service, N.H., *Type 2 diabetes: prevention and management of foot problems*. 2004, National Institutes of Health and Clinical Excellence: London.
10. Boulton, A., H. Connor, and P.R. Cavanagh, eds. *The Foot in Diabetes*. 1998, John Wiley & Sons.
11. Bharara, M., J. Cobb, and D. Claremont, *Thermography and thermometry in the assessment of diabetic neuropathic foot: A case for furthering the role of thermal techniques.* International Journal of Lower Extremity Wounds, 2006. **5**(4): p. 250-260.
12. Reiber, G., *Diabetic foot care: financial implications and practical guidelines.* Diabetes Care, 1992. **15**(Supplement 1): p. 29-31.
13. Bharara, M., J. Schoess, and D.G. Armstrong, *Coming events cast their shadows before: detecting inflammation in the acute diabetic foot and the foot in remission.* Diabetes/metabolism research and reviews, 2012. **28 Suppl 1**: p. 15-20.
14. Nishide, K., et al., *Ultrasonographic and thermographic screening for latent inflammation in diabetic foot callus.* Diabetes Res Clin Pract, 2009. **85**(3): p. 304-9.
15. Bagavathiappan, S., et al., *Correlation between plantar foot temperature and diabetic neuropathy: a case study by using an infrared thermal imaging technique.* Journal of diabetes science and technology, 2010. **4**(6): p. 1386-92.
16. Ring, F., *Thermal imaging today and its relevance to diabetes.* Journal of diabetes science and technology, 2010. **4**(4): p. 857-62.
17. Roback, K., M. Johansson, and A. Starkhammar, *Feasibility of a thermographic method for early detection of foot disorders in diabetes.* Diabetes Technol Ther, 2009. **11**(10): p. 663-7.
18. Nagase, T., et al., *Variations of plantar thermographic patterns in normal controls and non-ulcer diabetic patients: Novel classification using angiosome concept.* J Plast Reconstr Aesthet Surg.
19. Bharara, M., et al., *Wound Inflammatory Index: A "Proof of Concept" Study to Assess Wound Healing Trajectory.* Journal of Diabetes Science & Technology, 2010. **4**(4): p. 773-779.
20. Bharara, M., V. Viswanathan, and J.E. Cobb, *Warm immersion recovery test in assessment of diabetic neuropathy--a proof of concept study.* Int Wound J, 2008. **5**(4): p. 570-6.