Imaging Techniques used for Wound Healing Assessment

Poh Hong Tan[1,2*]

[1]*Department of Burns and Plastics, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom*

[2]*The Scar Free Foundation Centre for Burns Research, University Hospital Birmingham Foundation Trust, Birmingham, United Kingdom*

Abstract

Aim: The purpose of this study is to provide a short description of the performance of various non-invasive Imaging techniques used for wound healing assessment described in the literature.

Objective: Assessment of wounds carries both prognostic and diagnostic value thus determines treatment strategies and objectively examines the efficacy of emerging and novel wound therapies. Therefore, the aim of this article is to evaluate several objective imaging based wound assessment techniques.

Methods: Electronic databases were searched for all available publications on the use of wound assessment devices on human and artificial wounds using appropriate search terms. The primary outcome was the reliability and reproducibility of measurement whilst the secondary outcome was the feasibility of the instrument. All studies underwent Quality Assessment of Diagnostic Accuracy Studies (QUADAS) to examine the quality of data.

Results: Forty-four articles were identified evaluating 11 instruments which were divided acute wound measuring devices and chronic wound measuring devices. Average QUADAS score was 11 with lowest at 9 and highest 14. The highest performing instrument for acute wound healing was multi-photon tomography. It provides morphological assessment at a histological level, and details physiological status through optical redox ratio auto-fluorescence. However, its current high cost would therefore limit its use to research rather than clinical setting. The 3D system is ideal for wound assessment of chronic wounds. The combination of portability and ease of use outperforms hyper-spectral imaging, OCT and MPT, whilst its accuracy is superior to 2D imaging.

Discussion/Conclusion: This was an article which compared the performance of instruments for chronic and acute wounds. The article provides an extension into three further articles which provide a more in-depth review of the performances of the described instrument.

Keywords: Wound healing • Objective measurement • Mobile application • Wound measuring device

Introduction

An objective evaluation of wounds is necessary to determine the progression of healing which guides treatment strategies.

UK Standards

In the UK, majority of wound care is in the community and is dependent on a subjective wound assessment. In a study on community based surgical wound management, Guest, et al. identified a number of emerging concerns [1].

- Variations in documentation standards and terminology used for both wound nature and infection
- Lack of secondary care and specialist advice
- Apparent lack of treatment planning, reassessment, and revaluation of care.

This has resulted in increased re-admission rates and patient morbidity. The study highlights the need for common definition reporting standards, integration of care across providers and early senior involvement.

Research problem: The evidence above suggest that an objective, validated wound assessment method is required in wound care [2]. However current practices are based on clinical assessment, wound assessment scoring and histological studies which can be subjective and vulnerable to bias.

Clinical assessment: The most common method of wound assessment is clinical. Unfortunately, due to the nature of wound assessment, inaccuracies and inconsistency can be found Kantor and Margolis found inter-rater variability due to body natural curvature when assessing wound circumference [3], whilst Johnson and millet demonstrated lack of reproducibility between clinicians when objectively and subjectively monitoring wound progression by assessing depth [3]. In another study by Mekkes and Wastehof, intra and inter variation was noted when reporting visual estimation of percentage area [4]. Evidently wound assessment with this method has a degree of unavoidable bias

Assessment tools: Wound staging and assessment tools were developed in hopes to unify and develop better reliability between wound assessments. In a systematic review by Phillen, et al. [5], which assessed the validity of 10 different clinical tools including Pressure Ulcer Scale for Healing (PUSH), Pressure sore Status tool assessment Scale (SS) and Sussman wound healing tool, none achieved all the requirements for instrument validation with respect to content and criterion validity, intra and interrater reliability and sensitivity to change, although PUSH tool and PSST were validated to greatest extent [5]. The evidence suggests that the dependency of a subjective assessment and lack of an establish gold standard to compare, significantly limits its performance [5].

Histological assessment: Histo-pathological study remains the most commonly used in wound healing research. Whilst it is consider a gold standard [6], there are a number of potential disadvantages. First, an ideal grading system for wound healing has not been established, therefore results could defer depending on clinical site [7-9]. Second, serial evaluation cannot be achieved due to local destruction of tissues which may worsen the wound. Third, increased morbidity of the patient due to infection and pain. Finally, lack of appreciation of physiological changes (deoxy/oxy-haemoglobin and water fraction) in wound healing due to the static nature of the analysis. [7-9].

Methodology

A systematic literature search was done using PICO strategy. Adults and animals with acute, chronic, burn or grafted wounds was the population, with histo-pathological analysis or clinical assessment of healthy tissue as the comparator, where available. The primary outcome was the validity and reliability of the instrument whist the secondary outcomes was its feasibility such as speed of assessment, ease of use and cost of tool. ASSIA, Cochrane library, EM base, Medline, PubMed and the knowledge network Scotland were systematically searched with appropriate mesh terms employed. All studies underwent Quality Assessment of Diagnostic Accuracy Studies (QUADAS) to ensure quality of data.

Results

A total of 773 articles were produced from the initial search, and an addition 153 was added when examining systematic reviews/metanalysis of similar nature. In combination a total of 926 articles were generated after duplicated were removed. After filtering by review of titles and abstracts 203 suitable articles were chosen and 723 articles were excluded. Full articles were obtained, and a further 91 articles were removed after evaluating the full text. A total of 44 articles were selected in the final review. The selection process was outlines in (Figure 1) all studies were published from 1998 and onwards. The flow chart of inclusion and exclusion studies is presented in the Figure 1 below. The average QUADAS score was 13 with a range of 9 to 14.

Acute wounds

Five instruments were identified in the literature. This includes Optical Coherence Tomography (OCT), Confocal Microscopy (CLSM), Ultrasound Multi-photon Tomography (MPT), Laser Speckle and 2D imaging. All instruments had an objective method of measuring and were comparable to histological findings. OCT, CLSM, US and MPT directly identifies tissue morphology whilst laser speckle determined physiological changes. 2D imaging provided a global image of superficial structure but no details of the underlying structures. OCT had mixed evidence on measuring vascularization and CLSM was hindered by heavy slough build up. Ultrasound has the largest field of view 22 mm × 22 mm [10], followed by Optical coherence tomography 10 mm × 10 mm [11], confocal microscopy 8 mm × 8 mm [12,13], then multi-photon and laser speckle at 4 mm × 4 mm and 6 mm respectively. 2D imaging had no particular limitation to area of view although accuracy was inversely proportional to wound size [14]. US utilised sound waves which penetrate tissue up to 20 mm in depth, whilst
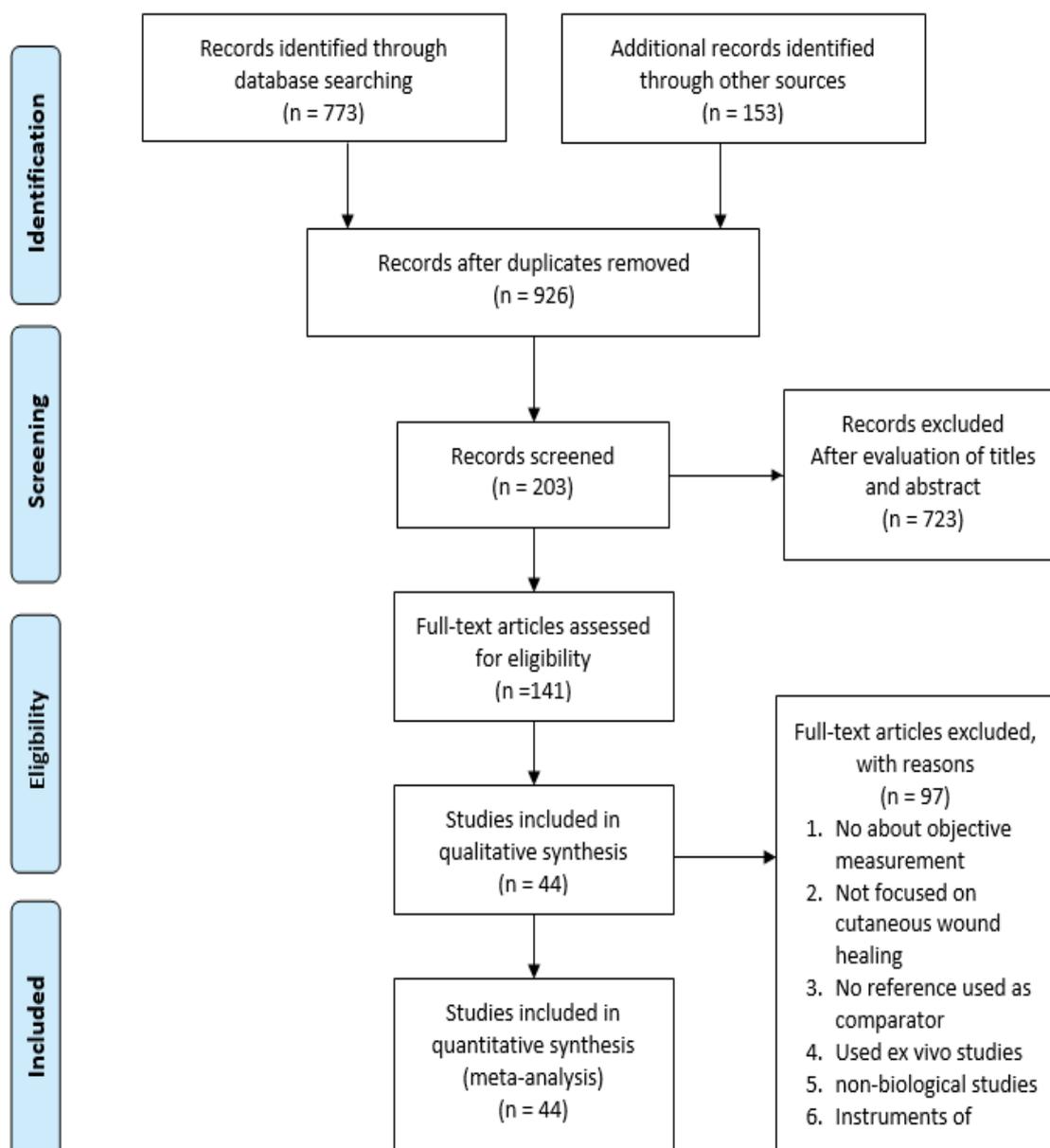

Figure 1. Prisma table.

OCT, CLSM, MPT and Laser Speckle were dependent on light technology and formed an image *via* post processing techniques. Light waves tend to have much better resolution with more defined image [12,15]. MPT had the most superior imagine quality. There was a large variation in cost, MPT was £180K, OCT £35K-£150K, US £6K, CLSM £22K whilst laser speckle and 2D imaging was in sub £100.

The highest performing instrument for acute wound healing was multi-photon tomography. In addition to morphological assessment at a histological level, it details the physiological status through optical redox ratio auto-fluorescence. However, its current high cost would therefore limit its use to research rather than clinical setting.

Chronic wounds

Five instruments were used to assess chronic wound healing. They were, OCT, MPT, Hyper-spectral imaging, 3D and 2D imaging. Although all the instruments produced repeatable, reliable result over time, hyper-spectral and 3D imaging had the strongest potential.

Hyper-spectral imaging was particularly useful in measuring oxy and deoxy-hemoglobin levels against a healing index which could accurately predict wound progress with high sensitivity and specificity [16]. Unfortunately, there was only one study included in this article and thus the reliability of the instrument could not be determined.

3D imaging is a highly portable system which detects small changes of wound size, oedema and level of granulation over time [17], making it an ideal tool for longitudinal studies. When compared to planetary methods, it was significantly more accurate (3% to 5% SD compared to 20% SD for small wound [18] and had a similarly high interrater correlation (ICC=0.9867; P<0.001) [19]. In addition, the 3D system is simple to use with marginal difference in outcome between non expert and expert users [19]. Finally the 3D system was cheaper than the hyper-spectral system (£20k *vs.* £200k) [20,21].

The 3D system is ideal for wound assessment in the community. The combination of portability and ease of use outperforms hyper-spectral imaging, OCT and MPT, whilst its accuracy is superior to 2D imaging

Discussion

Wound healing assessment is complex; this article suggests the use of available medical devises. In addition to consistent objective wound healing measurements, the images can be easily shared amongst healthcare workers over the internet at different sites. Therefore, each patient can receive a more holistic multidisciplinary approach. Moreover, the use of pictures will enhance the documentation and enables healthcare workers to track changes in the wound over time increasing inter and intrarater correlation.

Most of the medical devices highlighted here are not new. In fact, many of them have been validated and are in use in different part of health care. OCT is extensively used in ophthalmology, dermatology and oncology owing to its capability to show cross sections of tissue layers with micrometer resolution [22]. While ultrasound technology have been used in all parts of medicine from breast surgery to urology as a diagnostic and therapeutic instrument [23]. The translation to cutaneous medicine should therefore show strong potential.

There have been several systematic reviews which aim to validate some of these instruments. Ud-din, et al. [24] outlined various applications of objective technologies for the assessment of wound healing through the different phases of repair. Jorgensen, et al. [25] on the other hand evaluated the evidence for accuracy, agreement, reliability and feasibility of area and volume measurement technology. Albeit not a novel idea, devices here present non-contact optical based devices only that is easy to use in both research and clinical work. We have also investigated several devices that were not featured in other systematic review.

Conclusion

Several such instruments were briefly described in this article with the best performing instrument highlighted. As part of a series of papers, this article provides a short preview of the three core articles titled "The performance of portable objective wound assessment tools: A systematic review", "Imaging techniques used for wound healing assessment: A systematic review Part 1 Chronic wounds" and "Imaging techniques used for wound healing assessment: A systematic review Part 2 Burns wounds" which details the performance of each instrument relative to its use for specific wound types.

References

1. Guest, Julian F, Graham W Fuller and Peter Vowden. "Costs and Outcomes in Evaluating Management of Unhealed Surgical Wounds in the Community in Clinical Practice in the UK: A Cohort Study." *BMJ Open* 8 (2018): 12.

2. Ud-Din, Sara and Ardeshir Bayat. "Non-Invasive Objective Devices for Monitoring the Inflammatory, Proliferative and Remodelling Phases of Cutaneous Wound Healing and Skin Scarring." *Exp Dermatol*. 25 (2016): 579-85.

3. Kantor, J and DJ Margolis. "Efficacy and Prognostic Value of Simple Wound Measurements." *Arch Dermatol* 134 (1998): 1571-4.

4. Johnson, M and R. Miller. "Measuring Healing in Leg Ulcers: Practice Considerations." *Appl Nurs Res* 9 (1996): 204-8.

5. Pillen, Heath, Michelle Miller, Jolene Thomas and Phillip J Puckridge, et al. "Assessment of Wound Healing:Validity, Reliability and Sensitivity of Available Instruments." *Wound Pract Res J Aust* 2009.

6. Frykberg, Robert G and Jaminelli Banks. "Challenges in the Treatment of Chronic Wounds." *Adv Wound Care* 4 (2015): 560-582.

7. Sultana, Jachmen, Motiur Rahman Molla, Mohammed Kamal, M. Shahidullah, and et al. "Histological Differences in Wound Healing in Maxillofacial Region in Patients with or without Risk Factors." *Bangladesh J Pathol* (1970).

8. Lemo, Niksa, Geneviève Marignac, Edouard Reyes-Gomez and Thomas Lilin, et al. "Cutaneous Reepithelialization and Wound Contraction after Skin Biopsies in Rabbits: A mathematical Model forHealing and Remodelling Index." *Vet Arh* 80 (2010): 637-652.

9. Gupta, Akriti and Pramod Kumar. "Assessment of the Histological State of the Healing Wound." *Plast Aesthetic Res* (2015).

10. Rippon, MG, K. Springett, R. Walmsley and K. Patrick, et al. "Ultrasound Assessment of Skin and Wound Tissue: Comparison with Histology." *Ski Res Technol* 4 (1998): 147-54.

11. Gong, Peijun, Shaghayegh Es'haghian, Fiona M Wood and David D Sampson, et al. "Optical Coherence Tomography Angiography for Longitudinal Monitoring of Vascular Changes in Human Cutaneous Burns." *Exp Derma* 25 (2016): 722-4.

12. Lange-Asschenfeldt, Susanne, Adrienne Bob, Dorothea Terhorst and Martina Ulrich, et al."Applicability of Confocal Laser Scanning Microscopy for Evaluation and Monitoring of Cutaneous Wound Healing." *J Biomed Opt* 17 (2012): 076016.

13. Altintas, Ahmet A, Merlin Guggenheim, Mehmet A Altintas and Peymaneh Amini, et al. "To Heal or Not to Heal: Predictive Value of *In Vivo* Reflectance-Mode Confocal Microscopy in Assessing Healing Course of Human Burn Wounds." *J Burn Care Res* 30 (2009): 1007-12.

14. Bhedi, Amul, Atul K. Saxena, Ravi Gadani, and Ritesh Patel. "Digital Photography and Transparency-Based Methods for Measuring Wound Surface Area." *Indian J Surg* 75 (2013): 111-114.

15. Iris, Riemann, Alexander Ehlers, Ronan LeHarzic and Sven Martin, et al.

"*In vivo* Multiphoton Tomography of Skin During Wound Healing and Scar Formation." *Multiphot Microsc Biomed Sci* 6422 (2007): 644226.

16. Ponticorvo, Adrien, David M Burmeister, Rebecca Rowland and Melissa Baldado, et al., "Quantitative Long term Measurements of Burns in a Rat Model using Spatial Frequency Domain Imaging (SFDI) and Laser Speckle Imaging (LSI)." *Lasers Surg Med* 49 (2017).

17. Körber, Andreas, Jost Rietkötter, Stephan Grabbe and Joachim Dissemond. "Three-Dimensional Documentation of Wound Healing: First Results of a New Objective Method for Measurement." *J Dtsch Dermatol Ges* (2006).

18. Plassmann, Pand TD Jones. "MAVIS: A Non-Invasive Instrument to Measure Area and Volume of Wounds."*Med Eng Phys* 20 (1998).

19. Davis, A J, J Nishimura, J Seton and BL Goodman, et al. "Repeatability and Clinical Utility in Stereo Photogrammetric Measurements of Wounds." *J Wound Care* 22 (2013): 94-7.

20. Sirazitdinova, Ekaterina and Thomas M. Deserno. "System Design for 3D Wound Imaging using Low-Cost Mobile Devices*." Imaging Informatics* (2017).

21. Adão, Telmo, Jonáš Hruška, Luís Pádua and José Bessa, et al. "Hyperspectral Imaging: A Review on Uav Based Sensors, Data Processing and Applications for Agriculture and Forestry." *Remote Sens* 9 (2017).

22. Adhi, Mehreen and Jay S Duker. "Optical coherence tomography-current and future applications," *Curr Opin Ophthalmol* 24 (2013).

23. Barnet,t SB, GR Terhaar, MC Ziskin and HD Rott, et al. "International Recommendations and Guidelines for the Safe use of Diagnostic Ultrasound in Medicine." *Ultrasound Med Biol* (2000).

24. Ud-Din, Sara, Nicholas S Greaves, Anil Sebastian and Mohamed Baguneid, et al. "Non-Invasive Device Readouts Validated by Immuno-Histochemical Analysis Enable Objective Quantitative Assessment of Acute Wound Healing in Human Skin." *Wound Repair Regen*. 26 (2015).

25. Bisgaard, Jørgensen Line, Jens A Sørensen, Gregor Be Jemec, and Knud B Yderstraede. "Methods to Assess Area and Volume of Wounds-A Systematic Review." *Int Wound J* 13 (2016).

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