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TECHNICAL REPORT

A literature review of different pressure ulcer models from 1942-2005 and the development of an ideal animal model

P. K. T. Nguyen¹, A-L. Smith² and K. J. Reynolds¹

¹*School of Informatics and Engineering, Flinders University, Adelaide, Australia*

²*Flinders Biomedical Engineering, Flinders Medical Centre, Adelaide, Australia*

Abstract

The literature from 1942-2005 was reviewed in order to determine an inexpensive animal model which can closely mimic pressure ulcers seen in humans of varying ages, without the need for surgical procedures. Two animal models for producing pressure ulcers were found to be inexpensive: pigs to mimic pressure ulcers in young humans due to their fixed skin, and rats to mimic pressure ulcers in the elderly due to their loose skin. The methods which were found to be inexpensive, reproducible, non-invasive and easy to carry out without the need of a surgeon or specialist were the use of magnets for rat models and the use of a cast placed over a bony prominence for pig models.

Key words animal, model, pressure, sore

Introduction

Pressure ulcers (also known as bedsores or decubitus) affect the immobilised (e.g. paraplegics and quadriplegics), the elderly, and those who are bed-ridden due to sickness. These lesions are caused by persisting pressure over bony prominences such as the sacrum and ischii^{1,2}.

It is evident from recent findings that pressure ulcers are due to ischemia-reperfusion cycles and not just local applied pressure alone¹. Ischemia is a restriction of blood supply and results from localised applied pressure. Due to the lack of blood supply to the tissue, there is no oxygen being delivered therefore placing the tissue into hypoxia or anoxia. According to Seiler & Stahelin's experiment³, 20.3 kPa (200 g/cm²) average skin pressure at bony prominences resulted in complete anoxia. Tissue necrosis then followed a short time afterwards. From their results, a skin pressure as low as 6.1 – 8.1 kPa (60-80 g/cm²) was sufficient to slowly reduce the blood supply and rapidly decline skin oxygen availability. The authors concluded from their experiment that skin oxygen availability to areas over hard sites is highly sensitive to pressure, and a pressure above 44g/cm²; the arteriolar occlusion pressure, would initiate the cascade of pressure ulcer development.

Apart from ischemia as a result of applied external pressure, lymph flow in the local area is also inhibited. When lymph flow is inhibited, there is an accumulation of metabolic waste products and enzymes that result in tissue necrosis⁴. An applied external pressure of 10 kPa (75 mmHg) is sufficient to stop lymph clearance, and at any pressure where a vessel collapses, lymph flow is severely decreased. Impaired lymph flow is a contributor to pressure ulcer development⁶.

Pressure ulcers are a problem in veterinary medicine as well as in human medicine⁵, therefore animal models can be used to mimic pressure wounds in humans.

This paper seeks to identify the ideal animal model for studying early stage pressure ulcers by reviewing the literature from 1942 – 2005. The ideal model will be one which can closely mimic pressure ulcers seen in humans of varying ages, is inexpensive and does not involve any surgical procedures.

Discussion

Pressure ulcer models

There have been three main pressure ulcer models put forward to describe pressure ulcer development. These models are known as: top-to-bottom, bottom-to-top, and the middle model¹.

The bottom-to-top model was used to suggest that although pressure is exerted on the surface, muscle degenerates from the bone upwards towards the skin surface¹. Groth's experiment⁷ resulted in muscle damage in the rabbits which demonstrated that early stage pressure wounds may not show any damage to the surface, but initial

Corresponding author: Phuong K. T. Nguyen, PO Box 192, Parramatta, NSW, 2124, Australia

Tel: 0421 660 629, Email: pdo@zoll.com.au

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damage located in the muscle. Groth's conclusions described a bottom-to-top model⁷. Many other authors seeking to understand the development of pressure ulcers also had results suggesting the existence of a bottom-to-top model⁶⁻⁹. In 1998, Goldstein & Sanders¹⁰ observed the skin's response to repetitive mechanical stress in pigs. Their results strongly supported the top-to-bottom model instead, but did not take into account ischemia-reperfusion injury located in muscle tissues as did Seiler *et al.*³ and Groth⁶.

Kosiak *et al.*'s study in 1958¹⁶ found pressures under the ischia were in excess of mean capillary pressure for human subjects seated upright on flat hard surfaces, hard contoured surfaces and flat padded surfaces. The authors concluded that the only means of reducing pressure to the ischia was to have an alternating pressure contoured chair¹⁶. However unlike Seiler *et al.* and Groth's studies, the alternating pressure would most likely contribute to the ischemia-reperfusion injury which would exacerbate pressure ulcer development.

The top-to-bottom model of pressure ulcer formation suggested that pressure ulcers were due to pressure exerted from the top surface of the skin progressively extending deeper to the bone¹. Goldstein & Sanders' paper¹⁰ was the only literature found for this review in support of the top-to-bottom model, and was the only paper which investigated the effects of shear forces and loading on skin. The top-to-bottom model is a plausible model to describe pressure ulcer development; however there has been more evidence suggesting initial damage occurs in the muscle tissues and not skin surfaces.

Recently, the middle-model was established. This middle model suggested that degeneration occurs in the middle layer and spreads both to deeper and more superficial tissue¹. Looking at the histology of pressure ulcers, Salcido *et al.*^{8,11} used a computer controlled surface pressure system which produced pressure ulcers of various stages, depending on the amount and duration of pressure, in fuzzy rat trochanter regions. Fuzzy rats are hairless due to a hypotrichotic mutation¹². This experiment consisted of a constant pressure of 19.3 kPa (145 mmHg) applied for 6 hours duration at each session for 5 consecutive daily pressure sessions. This paper described necrosis of the panniculus carnosus, a thin layer of muscle beneath the skin, and superficial adipose tissue over the trochanter regions, but no epidermal damage in early stages of pressure sore development.

Evidence for early pressure wound formation

Arao *et al.*¹³ excised skin tissues containing healthy and damaged areas from an 87 year old human female 4 hours after death by cerebral infarction. The pressure wound over the sacrum was identified as a stage 2 pressure sore. Arao *et al.*¹³ suggested from their findings that the dermal papillae had morphological features which are characteristic of pressure sore development in comparison to healthy tissue. The papillae are responsible for the exchange of oxygen, nutrients and waste products between the dermis and epidermis via its finger-like projections which increase surface area. Comparing the healthy region with the damaged area, it was found that no papillae or collagen

fibrils were intact in the damaged area. This is the most likely cause of early stage pressure ulcer formation as the papillae may be destroyed without the dermis being destroyed, however papillae in aged skin tend to be flat with or without pressure, therefore it may be difficult to determine whether the absence of papillae in aged skin are due to aged skin or early pressure ulcer formation¹⁴. The paper did not mention however, whether it was possible that changes in papillae can be a sign of early stage 1 pressure ulcer development.

Pressure ulcers in animals

Animals used in experiments tend to be healthy, well fed, and mobile. However, some animals such as canines, horses and cattle are prone to developing pressure ulcers⁶ in certain conditions (e.g. dogs with thin skin and low body fat, horses with poorly fitted saddles and cattle confined to hard concrete floors). Greyhounds in particular develop pressure ulcers mainly due to their thin skin⁶.

Animal models – induced ulcers

The most common animals used to model pressure ulcer were rats, mice, rabbits and pigs. To model pressure ulcers in animals that appropriately mimic the pressure wounds in humans of varying ages, more than one type of animal can be used. For young humans, pigs can be used due to their fixed skin. For more elderly humans, the skin is much thinner and hence rats can be used due to their loose skin. Furthermore, these two animals are relatively inexpensive in comparison to using greyhounds and hence can be used on a large scale study. The cost for keeping pigs is 25 times the cost of keeping rats. Canines are not kept due to their higher cost. In Kosiak's study of decubitus ulcers in 1961, albino rats were used to create ischemic ulcers using constrictive dressing¹⁷. Fuzzy rats are similar to albino rats since they both have thin skin and red eyes however fuzzy rats¹² are not preferred because they have poorly developed skin and cystic follicles that make it difficult to model the elderly. Kosiak's study did not mention why albino rats were chosen over standard rats, one reason could be that standard rats are easier to source and hence more inexpensive. Although mice and rats cost approximately the same, rats are preferable because of their larger size allowing easier handling for measurements. Since the cost of keeping the animals remains the same despite their age, younger pigs would be preferred allowing easier handling¹⁰.

Kosiak used dogs in their study of ischemic ulcers¹⁸. It is not clear why the authors chose canines over other animal models, but in the last 1950's canines were more widely used and the cost using canines was not exorbitant. Furthermore, Kosiak's experimental set up was large and cumbersome as it required the canines to remain under the pressure apparatus for long periods of time (1-12 hours). Swaim *et al.*⁵ used greyhounds in their study of pressure ulcers because of their thin skin and their susceptibility to pressure ulcer development. The authors placed a limb in a cast that was designed to apply pressure to the site of the bony prominence. This method is inexpensive and can be used on pigs. Similarly, Sundin *et al.*¹⁵ applied a cyclic

pressure on the scapulae of pigs to create pressure ulcers. The use of a cast as in Swaim *et al*'s study, however, is more of a realistic scenario since the pigs would still be able to move around after the application of the cast causing the reperfusion injury required to produce a pressure ulcer as well as produce some friction to the surface of the skin.

Stadler *et al*⁹ used two magnets to hold a pinch of skin in between (i.e. forming a bridge) to produce pressure ulcers in mice. It produced ischemia-reperfusion cycles by removing and reapplying the magnets. This method is reproducible, inexpensive and can be used on rats.

The animals chosen for the ideal pressure ulcer model in this paper; rats and pigs, would be expected to display different results as the two animals are of different size and species. The main issue with using animal models is that the results are influenced by many factors such as: age of the subject, size of the subject, how nourished and hydrated the subject is and what part of the body is being measured. Although animals can mimic the development of pressure ulcers, it is still important that these factors are considered when using any animal models in pressure ulcer studies.

Conclusion

From the reviewed literature it can be concluded that rats would be suitable for modelling skin in older humans and pigs would be suitable for modelling skin in young humans. The two animals are inexpensive and can be used for large scale studies. The two methods which were found to be inexpensive, non-invasive, reproducible and easy to carry out without the need of a surgeon or specialist were the use of magnets as described by Salcido *et al*¹¹ and the use of a cast over a bony prominence as described by Swaim *et al*⁵.

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