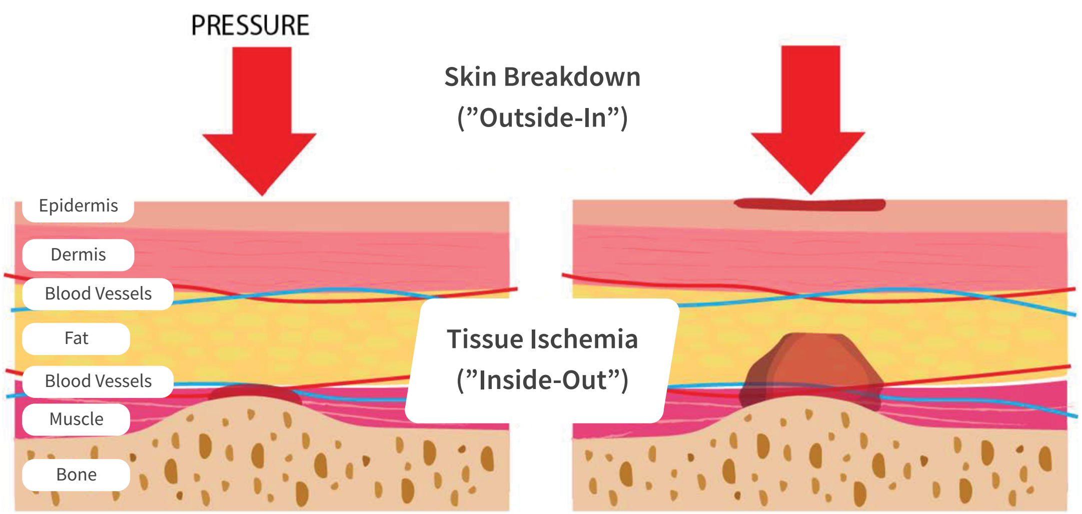
Background

Pressure injuries are a severe breakdown in soft tissue around bony regions of the body that are commonly seen in people with reduced mobility or sensation. They can originate at the surface of the skin and progress inwards; or they can originate at deep bone-muscle interfaces and progress outwards.

Factors contributing to externally developing ulcers are friction, moisture, nutrition and hygiene. The primary factor associated with internally originating ulcers is the pressure on and around tissue surrounding bony prominences. Pressure in deep tissue mechanically deforms the tissue and decreases oxygenation, both of which lead to irreversible tissue damage.



Rehabtronics has developed a neurostimulation technology that both reforms the tissue and restores blood circulation and tissue oxygenation.

Study Overview

Rehabtronics has developed a proprietary neurostimulation protocol called 'IES'. IES has been integrated into the Prelivia IES1 device. It has been established that a pressure injury may form via extrinsic and intrinsic factors. Externally, sustained pressure over bony prominences (extrinsic) and a lack of blood circulation, tissue oxygenation and tissue perfusion (intrinsic). Prelivia is the first technology to addresses both factors.

In a series of animal, human, and clinical studies it has been shown that 'IES' aids in:

- redistributing pressure,
- reforming compressed muscle tissue,
- increasing tissue oxygenation by 28%, and
- reduced deep tissue damage by 80%.

Clinical studies have demonstrated that Prelivia is safe and easy to deploy in hospital settings. Use by patients and health care workers demonstrates that there are no barriers to implementation and acceptance by all stakeholders.

Study Results

Preclinical trials were performed in animal models to demonstrate that IES can:

1) redistribute pressure around bony prominences
2) increase tissue oxygenation
3) reduce and/or eliminate the formation of deep tissue injury

Sustained pressure is an essential component of deep tissue injury. Therefore, the ability to disperse pressure by redistribution away from the focal point (i.e. at the site of tissue contact with bony prominences) is a key step in the prevention of one of the main underlying causes of PUs.

Blood Circulation and Tissue Oxygenation

IES treatment was also associated with an in increase in blood circulation (using functional magnetic resonance imaging) and a concomitant 28% increase in tissue oxygenation (See Figure 2) [Gyawali, et al, 2011] in both animal models and human subjects.

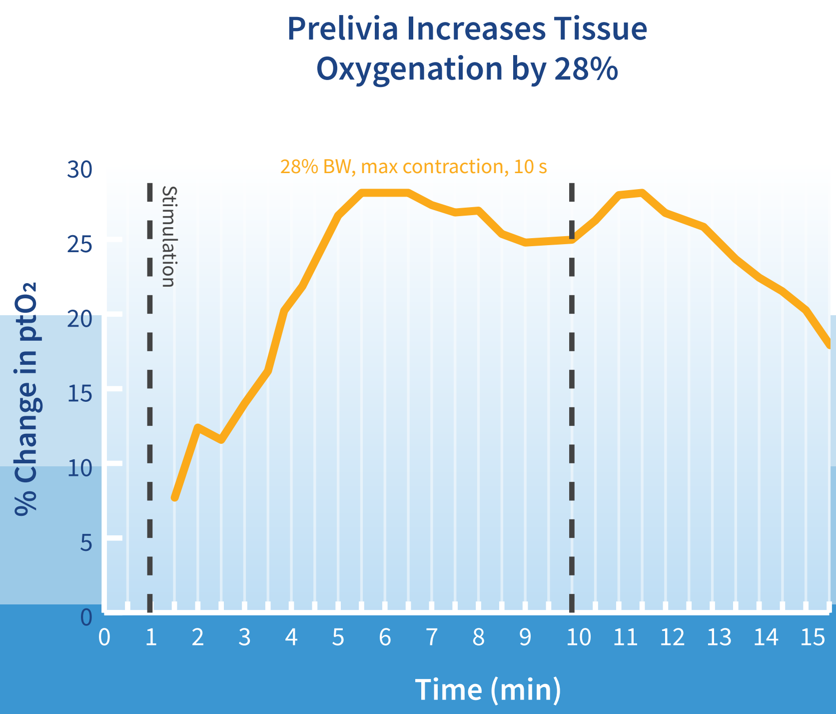


Figure 2: In a pre-clinical study where a 10 second IES pulse was applied, tissue oxygenation increased by 27.7%. The increase in tissue oxygenation began to decline substantially after 10 minutes. Prelivia stimulates periodically to optimize tissue oxygenation. [adapted from Gyawali et al, 2011]

Studies in able-bodied individuals with healthy muscles provided similar results, suggesting that IES is effective in counteracting the mechanical and vascular pathways leading to deep tissue injury even in both atrophied and healthy muscle tissue [Solis et al, 2011].

Deep Tissue Injury Formation

Using a pig model of deep tissue injury, IES significantly reduced deep tissue injury or eliminated its formation altogether as demonstrated through magnetic resonance imaging (MRI) (Figure 3A) and post-mortem histology (Figure 3B) [Solis et al, 2013]. Spinalized pigs were randomized into treatment (IES) or control groups. In both groups continuous pressure was applied to the hind quarters. Each pig's contralateral leg served as internal control. MRI images were taken at 2 weeks and 4 weeks. The pigs were euthanized, and tissue samples analyzed to corroborate MRI results (see Figure 4).

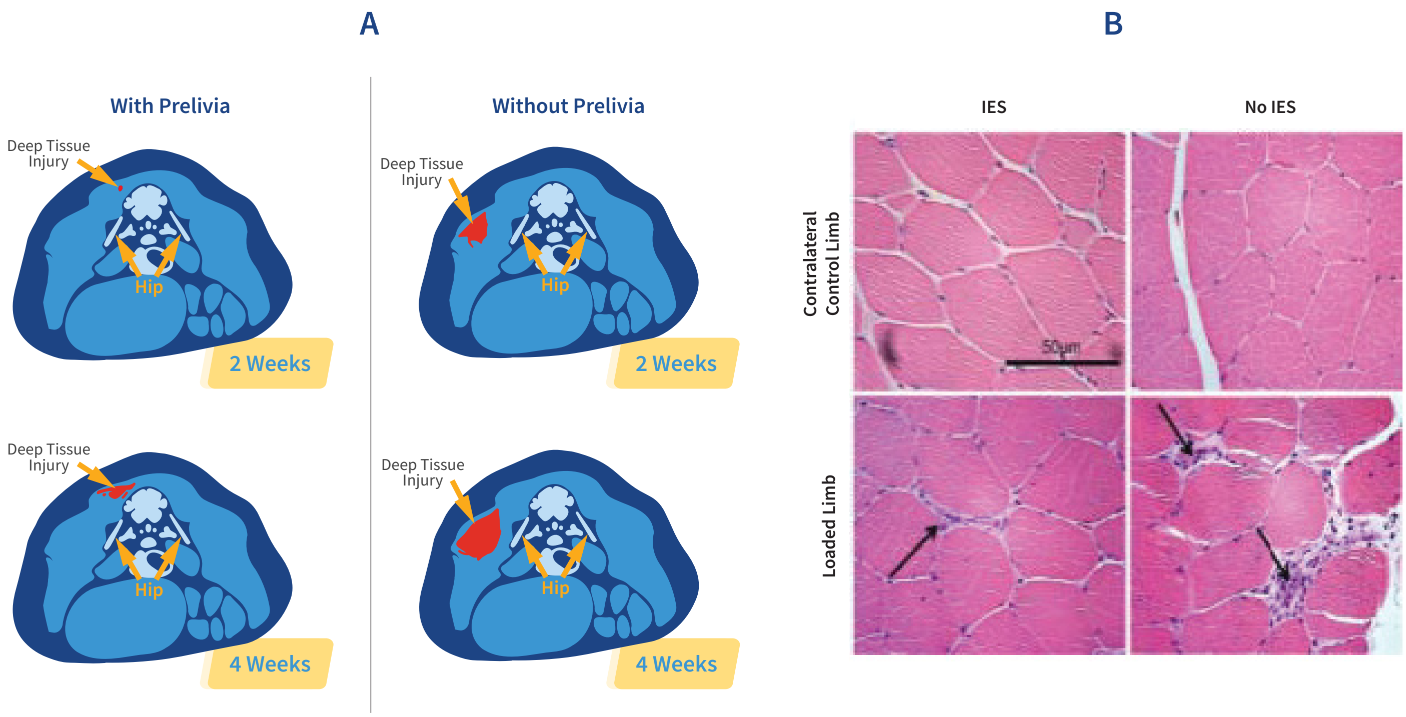


Figure 3: Pigs randomly assigned to 2 groups: control (no-IES) or treatment (IES). Animals in both groups were subjected to constant pressure being applied to one leg while the animal's other leg served as an internal control. Comparison of the amount of DTI estimated in one pig from each group (IES and noIES) after 2 and 4 weeks of daily loading. Yellow arrows indicate the location of muscle regions considered to contain DTI (red regions). B) Muscle samples from the contralateral control and loaded muscles from one pig in the IES and No IES groups stained with hematoxylin and eosin. Arrows indicate location of high infiltration of inflammatory cells into the muscle tissue. [Adapted from: Solis I, 2013]

Pressure Relief, Reduction, and Redistribution

Gyawali *et al* conducted a study in people with spinal cord injury (SCI) and atrophied (deteriorated) muscles to test the ability of IES to redistribute pressure in tissue near bony prominences and increase tissue oxygenation throughout the compressed muscles. Application of IES successfully re-distributed pressure in tissue around bony prominences by 10-26% (See Figure 4)[ref].

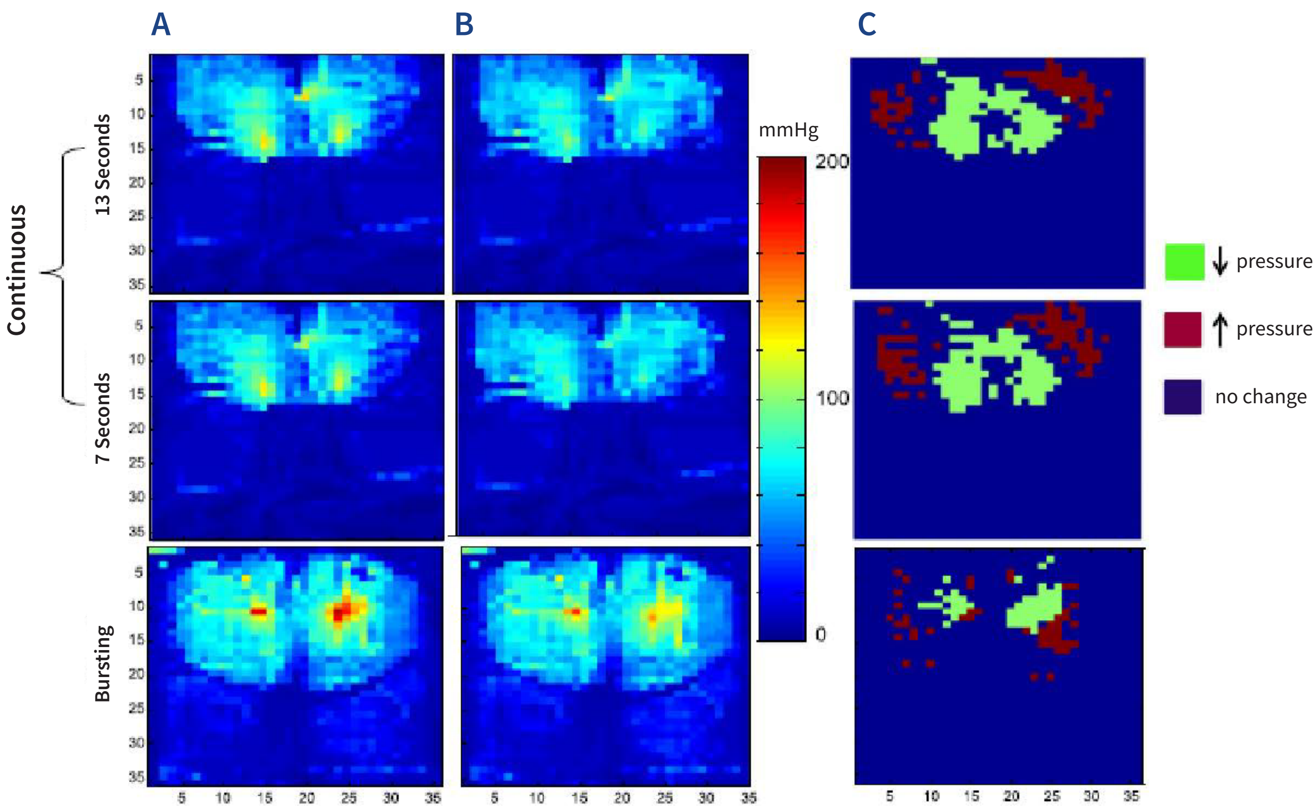


Figure 4: Pressure mapping of 1 study participant while seated. (A) At baseline. (B) IES in the 'ON' phase (stimulation phase). (C) Distribution of pressure change between baseline and IES 'ON' phase. Green, red, and blue indicate locations of significant decrease, increase, or no change in pressure, respectively. [Gyawali, et al, 2011]

In a pig model using intratissue pressure sensors (catheters), IES reduced and redistributed interfacial pressure [Solis et al, 2012]. Interfacial pressure is associated with the formation of deep tissue injuries. Importantly, IES shifted the focus of internal pressure away from the site of pressure load; i.e. it reduced the focal pressure at critical sites.

In another experimental model, rats were used to determine the effects of varying conditions of IES. Under anesthesia, an indenter was used to deliver a constant pressure equivalent to 18%, 28% or 38% ofbody weight. In some conditions, the load was released to simulate the standard turning protocol implemented by nurses at regular intervals to temporarily relieve pressure [Curtis et al, 2011]. Conventional treatment involving temporary pressure relief (i.e. turning) was not effective in reducing the extent of deep tissue injury. In contrast, IES under all levels of loading significantly reduced the extent of injury.

Clinical Safety and Acceptability

In a series of clinical studies 68 patients used Prelivia (at the time referred to as 'Smart-e-pants') for between 4 days and up to 2 months. Patients were in a variety of clinical settings including ICU [Kane et al, 2017], acute, sub-acute, and skilled nursing facilities [Ahmetovic, et al, 2015]. Inclusion criteria required that a subject was being treated as an in-patient, had intact innervation of the gluteal muscles, had intact skin in the gluteal region for at least three months prior to the study, and had the ability to provide informed consent (except in ICU where surrogate consent was accepted). No device related adverse events were observed.

Overall the system was found to be relatively easy to use by nurses. The intervention fit into existing nursing workflows with Prelivia pad changes coinciding with any one of existing skin inspections or other bowel and bladder routines. Prelivia required about 15 mins of nursing time which included study data collection. In the absence of study data collection, Prelivia takes <10 min of nursing time. Patients reported the system to be acceptable, comfortable, and not disruptive to sleep (see Figure 5).

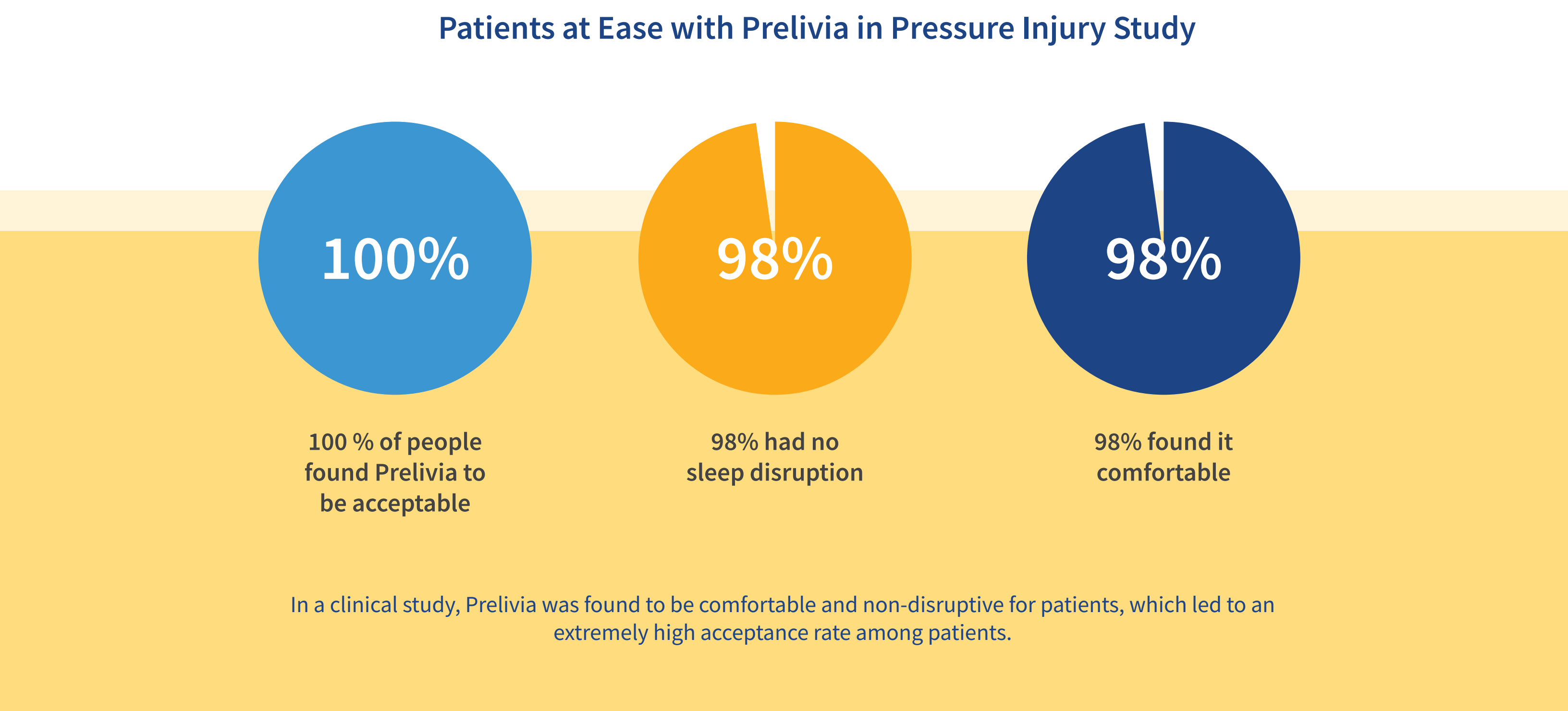


Figure 5: 100% of study participant who responded found Prelivia to be acceptable. 98% of respondents said Prelivia was not disruptive to sleep, and 98% said they found Prelivia comfortable.

Given concerns regarding staffing requirements, time to apply the IES system was measured and found that the time to apply was less than 10 minutes to apply and less than 5 minutes to remove in acute care settings. These data indicate that the use of Prelivia can be adopted in the clinical setting without requiring considerable investment in staff time or training.

Conclusion

Regardless of the point of origin, all pressure injuries involve deep tissue injury as a causal or coincidental factor. Research on Prelivia IES have focused on mitigating extrinsic and intrinsic factors in the prevention of tissue injury as a point of control to prevent the development of pressure injuries. Tables 1 and 2 summarize the research findings obtained using IES and Prelivia technology in human and animal studies.

Ease of use	Prelivia was found to be easy to integrate into existing workflows. Nursing found it relatively easy to use. It requires 10 mins or less of nursing time per shift.
Patient comfort	100% of patients reported Prelivia as acceptable. 98% reported it was comfortable and did not disrupt sleep.
Pressure re-distribution	IES redistributes pressure away from bony prominence and reduces interfacial pressure. IES was found to be more effective than temporary pressure relief (i.e patient turning) in animal models.
Increased blood circulation and tissue oxygenation	IES increases blood circulation and tissue oxygenation by 28%
Edema	IES reduces or prevents edema
Pressure-induced tissue injury	IES reduced pressure-induced deep tissue injury by 80% in animal models

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