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## Systematic Review

# EVALUATION OF THE EFFECTIVENESS OF COMBINATION ULTRASOUND TREATMENT AND BASIC CARE IN THE HEALING OF PRESSURE ULCERS: A SYSTEMATIC REVIEW

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#### Abstract

**Introduction:** When the pressure ulcer does not respond to established standard care, then international guidelines recommend the use of alternative forms of therapy such as electrical stimulation, negative pressure wound treatment, ultraviolet radiation, electromagnetic field therapy or ultrasound. Low and high frequency ultrasound is used to treat various types of chronic ulcers including venous, diabetic and pressure ulcers.

**Aim:** The aim of the present systematic review was to investigate the effectiveness of ultrasound in promoting the healing of pressure ulcers.

**Method and Material:** A systematic review was carried out in the electronic databases PubMed and Cochrane Library. Inclusion criteria were primary and secondary studies, whose sample were patients with pressure ulcers, regardless of age, published in English language of the last decade (2008-2018).

**Results:** The review revealed 5 articles that met the inclusion criteria. The results of these studies showed an advantage in the use of ultrasound for the treatment of pressure ulcers in relation to the standard wound care only.

**Conclusions:** The use of ultrasound seems to be a process which improves and accelerates the healing of pressure ulcers. The method of low and high frequency ultrasound in the treatment of chronic wounds, presents many advantages. It appears to be easy to use, painless, less stressful and better accepted by patients.

Keywords: Ultrasound therapy, ultrasound treatment, pressure ulcers, wound healing.

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## INTRODUCTION

Pressure ulcers (PrUs) represent a significant health challenge with a great number of people affected worldwide. Diseases that lead to restricted mobility and affect the blood and oxygen delivery to tissues play an especially important role in the development of PrUs. External factors such as pressure, friction, shear and moisture, as well as endogenous factors such as malnutrition, advanced age, hypotension, emotional stress, smoking and skin temperature, also play a combined role in the development of PrUs.<sup>1</sup>

When the pressure ulcer does not respond to standard wound care, then the international guidelines recommend the use of alternative forms of treatment such as electrical stimulation (ES), negative pressure wound treatment (NPWT), ultraviolet radiation, pulsed electromagnetic field therapy (PEMF) or ultrasound (US).<sup>2-7</sup> Ultrasound has been used by several health professionals for over 60 years. The biological effects on tissues exposed to ultrasound were first reported by Wood and Loomis in 1927.<sup>8</sup> The application of ultrasound for therapeutic purposes began in Germany in the late 1930s and in the United States in early 1940s.<sup>9</sup>

Studies of the last decade have shown that ultrasound treatment has a greater effect on wound healing than standard wound care only.<sup>1,10-13</sup>

#### The mechanism of action of ultrasound treatment

The therapeutic effects of ultrasound have been used by several researchers in the past. In 1960 Paul et al.,<sup>14</sup> describe the treatment of 23 patients with pressure ulcers using ultrasound. This study concluded that it would be extremely useful to further investigate this specific treatment. In 1985, 25 years later, McDiarmid et al.<sup>15</sup> published the first randomized clinical trial on the effects of ultrasound in healing of pressure ulcers. Although McDiarmid et al., could not show overall beneficial effect, they found that ultrasound treatment appeared to enhance the healing rate in a group of patients with infected surface ulcers.<sup>16</sup> In a randomized clinical study of Nussbaum et al., 1994<sup>17</sup> conducted in Canada, ultrasound treatment appeared Sotnikova et al. to have a greater effect on wound healing than standard wound care alone.

#### Types of ultrasound

According to Kloth and Niezgoda,<sup>9</sup> mechanical forces, such as ultrasound (US), can stimulate signal transduction pathways in tissue and produce a wide range of cellular effects that improve the healing of wounds.<sup>13</sup>

The ulcers can be managed with Low-Frequency Ultrasound (LFUS 22.5–40 kHz) or High-Frequency Ultrasound (HFUS; 1–3 MHz). The HFUS stimulates the conductivity of the cell membrane and increases the cell calcium concentration, which may promote significantly the activity of cells that are important for the wound healing. Moreover, the HFUS can stimulate the activity of macrophages and fibroblasts and activate the synthesis of collagen. In addition to this, the HFUS activates growth factors in wounds and promote neoangiogenesis.<sup>9,12,13</sup>

The Low Frequency Ultrasound has been used for the treatment of various types of chronic wounds including pressure ulcers.<sup>10,18,19</sup> The LFUS wound debridement offers a less traumatic, less painful surgical debridement, achieving destruction of the bacterial biomembrane, removing necrotic tissues, fibrosis, exudate and accelerating the formation of granulation tissue.<sup>20-22</sup> The LFUS waves act through two mechanisms: microcavitation and acoustic flow. Cavitation leads to cellular changes, destruction of periwound tissue in the ultrasound wave, also causes a rapid lysis of the necrotic tissue and ulceration fibrosis. The acoustic flow increases cell permeability and activates the intracellular secondary transport system which in turn causes an increase in collagen synthesis and production, growth factors, increase angiogenesis, macrophage response and fibrinolysis.<sup>9,10,18,22</sup>

#### AIM

The aim of this systematic review was to investigate the effectiveness of ultrasound in promoting the healing of pressure ulcers.

#### METHODOLOGY

Articles for this systematic review were searched in PubMed and Cochrane Library databases, with the keywords ultrasound therapy, ultrasound treatment, pressure ulcers, wound healing. Only Clinical Trials, Controlled Clinical Trials, Meta-Analysis, Multicenter Studies, Randomized Controlled Trials, Systematic Reviews, published in the last 10 years (2008-2018) were included.

Inclusion Criteria:

- Studies in English language
- Published in the last 10 years (2008-2018)
- Studies of patients of all ages

Exclusion criteria:

- To refer to animals
- Other language

Search results were: PubMed 23 studies of which 2 were Controlled Clinical Trials, 3 Multicenter Study, 8 Randomized Controlled Trial and 10 Systematic Reviews. In Cochrane Library found 24 studies, 2 Controlled Clinical Trials, 4 Multicenter Studies, 15 Randomized Controlled Trials, 3 Systematic Reviews. The 8 duplicates were excluded due to the title as well as 15 articles published before 2008. The 24 articles were remained. Of the 24 articles, 15 were excluded due to the title (venous ulcers, diabetic foot). Articles obtained for further evaluation were 9. There were excluded 4 articles due to non relevance to the subject. Finally 5 articles were remained for further research (flow chart). The description of these studies is presented in the table below.

### RESULTS

In a prospective randomized study by Bora et al.<sup>1</sup>, 27 treated neurological patients with stage II - IV pressure ulcers were studied using High Voltage Electrostimulation (15 patients) and Ultrasound (12 patients) for a period of 12 weeks. The researchers compared the effectiveness of these two methods in the treatment of pressure ulcers. A statistically significant reduction in pressure ulcer was found in both treatment methods Sotnikova et al. with p < 0.001. However, the limitations of this study indicate that there was no homogeneity in the sample in terms of classification and ulcer surface due to randomization, plus the absent of the control group.

In a prospective randomized single blind study by Polak et al.<sup>13</sup>, the effectiveness between High Frequency Ultrasound and Electrostimulation was evaluated. The 77 patients with 88 stages II - IV pressure ulcers were studied. Patients were divided into 3 groups. The first group (28 patients) received the standard wound care only, the second group (25 patients) received the standard wound care with simultaneous use of ultrasound and the third group (24 patients) received the standard wound care with the electrostimulation. The results showed significant healing rates in all three groups, but the groups of methods tested had a statistically significant reduction in the surface area of pressure ulcers. A significant limitation was the short duration of monitoring the development of ulcers (4-6 weeks), the long duration of the study and especially the small sample of patients.

In another perspective, randomized, controlled clinical trial by Polak et al.<sup>12</sup>, the effectiveness of High Frequency Ultrasound in stage II and III pressure ulcers in combination with standard wound care versus standard wound care only was evaluated and compared. The 42 patients with 44 pressure ulcers were studied. The patients were divided into one group which received a standard wound care only (22 patients with 23 pressure ulcers) and a second group which received a standard wound care in combination with ultrasound (20 patients with 21 pressure ulcers). The duration of follow-up was 6 weeks. The combination of the standard wound care with the ultrasound showed statistically significant results in terms of the average reduction of the ulcer area, on a weekly basis, over a period of 6 weeks and on healing in 6 weeks. In addition, the combination of the standard wound care with the use of ultrasound appeared to be superior although there were no statistically significant results. The limitations of the study includes the lack of a control group (sham ultrasound), that the study was not blinded as well as the researchers' belief that the standard wound care of pressure ulcers varied between the four research centers that participated in the study.

In a pilot randomized controlled clinical trial of Maeshige et al.11, evaluated the effect of ultrasound compared with the standard wound care in the treatment of pressure ulcers. There were 5 elderly neurological patients, with 7 stage III and IV pressure ulcers, without local wound infection and extensive necrotic tissue as well as these patients did not have diabetes mellitus type 2 or peripheral arterial disease. The ultrasound treatment group consisted of 3 patients with 4 ulcers and the control group consisted of 2 patients with 3 ulcers. All patients underwent the standard wound care during the study. In period A, each pressure ulcer received the standard wound care only for 2-4 weeks. In period B, each pressure ulcer received the standard wound care in combination with ultrasound or the standard wound care with sham ultrasound for the same duration as an ABABA sequence (alternating periods A, B, A). The results showed superiority in the ultrasound treatment group in the specific time period compared to the control group. The authors cite as a limitation of the study the very small sample, although there is a predominant tendency in favor of combination treatment.

A prospective experimental study by Serena et al.<sup>10</sup>, assessed the effectiveness of non-touch low frequency ultrasound treatment (MIST Therapy) in reducing the bacterial colonization in stage III pressure ulcers and promoting the healing. This was a multicenter study with a total sample of 11 patients with chronic stage III pressure ulcers, who met criteria such as: wound volume up to 160 cm<sup>3</sup>, bacterial measurements > 105 CFU/g of tissue (without infection) as well as patients without clinical signs of acute ulcer infection, without head or neck injury and without malignancy in the wound bed. The bacterial load of the ulcer was measured before and 2 weeks after the MIST Therapy. All patients underwent the standard wound care during the study. No local antibiotics, antiseptics, analgesics and antimicrobial dressings were allowed. The results showed Sotnikova et al. that the bacterial load was significantly reduced with the MIST treatment. The Streptococcus G. showed different response and resistance. The authors cited the absence of a control group as a limitation of the study, although the non-touch low frequency ultrasound treatment was shown to reduce the bacterial load in the ulcer bed promoting the healing.

#### DISCUSSION

The results of this systematic review showed superiority in the use of ultrasound for the treatment of pressure ulcers in relation to the daily standard wound care. Different types of ultrasound are used for the same expected result. In particular, the high frequency ultrasound (HFUS) acts at the molecular level by stimulating a number of mechanisms that promote the healing process.<sup>1,11-13</sup> On the other hand, the low frequency ultrasound (LFUS) is mainly used for the non-traumatic removal of soft necrotic tissue and biofilm. The presence of the biofilm reduces the effectiveness of the systematic use of antibiotics. Furthermore, chronic ulcers due to microangiopathy and fibrosis prevent the absorption of local antimicrobial agents, thus creating the need for non-toxic methods of cleaning such wounds. Regardless of the type of ultrasound, it appears that this method improves and accelerates the healing.<sup>10,13,18</sup>

Of course, the studies have several methodological problems, which require the adoption of their results with caution and skepticism. A major problem is the small sample of patients used in each study as well as the lack of a common methodology and heterogeneity of ultrasound types.<sup>1,10-13</sup>

In the study by Polak et al.<sup>12</sup>, a total of 4 centers for elderly patients with pressure ulcers were used, where, as the authors emphasize, there is a possibility of different protocols in the daily standard wound care. In the studies of Bora et al.<sup>1</sup> and Serena et al.<sup>10</sup> there were no control group.

Due to different methodology, follow-up period, use of different types of ultrasound and small sample, one can not draw safe conclusions in favor of the use of ultrasound.

## LIMITATIONS

The limitations of this systematic review are the small number of studies, the search of the relevant bibliography in only two electronic databases and the fact that were used studies published in English language only. Another limitation is that the studies have been found that examine in addition to ultrasound and another method of therapeutic intervention such as electrostimulation. However, these studies gave superiority of ultrasound over the electrostimulation.<sup>1,13</sup>

#### CONCLUSIONS

In conclusion, the use of ultrasound in the treatment of pressure ulcers appears to promote healing of the ulcer. However, the existence of a few studies with a limited sample can not lead to a generalization of the findings. For this reason, it is proposed to make more primary and multicenter studies on the use of ultrasound in combination with the daily standard wound care that might enable safer conclusions. Searching in more electronic databases as well as studies in a language other than English, would probably yield a larger volume of studies on this topic.

Taking into account the results of relevant researches, the method of low and high frequency ultrasound in the treatment of chronic wounds, presents many advantages. It seems to be easy to use, painless, less stressful and better accepted by patients.

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# ANNEX



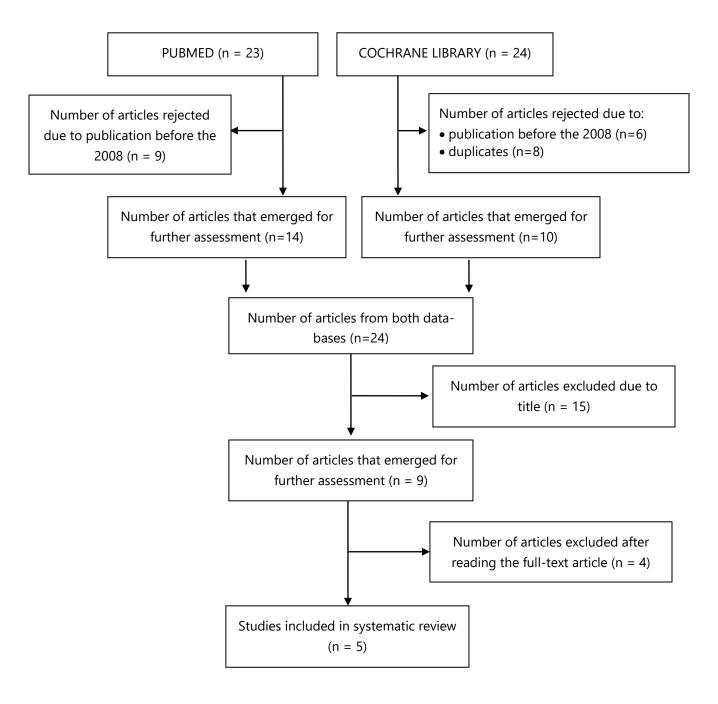


TABLE 1. The results of the systematic review on the effect of ultrasound on the healing of pressure ulcers.

AUTHOR- YEAR-	AIM	TYPE OF STUDY-	DATA	ANALYSIS	RESULTS	LIMITATIONS-
COUNTRY	Allvi	SAMPLE	COLLECTION	ANALISIS	RESULTS	CONCLUSIONS
1. Bora et al., 2017, Turkey.	Assessment and compar- ison of the effectiveness of High Voltage Elec- trical Stimu- lation (HVES) with ultra- sound (US), in treating Stage II-IV pressure ulcers of patients ad- mitted to a rehabilitation center.	Prospective, controlled trial. A total of pa- tients (n=27) with pressure ulcers Stage II- IV (n=47). Stage II: 14 (29,8%) Stage III: 26 (55,3%) Stage IV: 7 (14,9%) Patients in the US group (n= 12) Patients in the HVES group (n=15) Study duration: <b>not mentioned</b>	The patients' PrUs were classified ac- cording to the staging sys- tem developed by the National Pressure Ulcer Advisory Pan- el (NPUAP) <b>HVES device:</b> session dura- tion was 60', 3 times/week for 4-12 weeks. <b>US device:</b> 3 times per week for 4-12 weeks. All PrUs (sin- gle or multi- ple) were photographed and dimen- sions were calculated before and after treat- ment using wound evalu- ation scales.	Data analysis: SPSS version 15.0. The normality of distribution: Shapiro-Wilk test. Comparison of repetitive measurements within the groups: Paired-sample t test. Non- parametric data with non normal distri- bution: Wil- coxon signed rank test. Nominal vari- ables: Pearson x <sup>2</sup> test. Intragroup correlations between vari- ables: Spear- man correla- tion test. Multivariate linear regres- sion analysis was per- formed for variables af- fecting treat- ment out- comes. p <0,05 was considered statistically significant.	Statistically significant re- duction in pres- sure ulcer in both groups (43% in the HVES group and 63% in the US group (p <0.001). HVES group: Stage II: 17,40 $\rightarrow$ 11,40 (p=0,012) Stage III: 28,53 $\rightarrow$ 20,66 (p<0,001) Stage IV: 30,78 $\rightarrow$ 18,64 (p=0,020) US group: Stage II: 7,61 $\rightarrow$ 1,50 (p=0,041) Stage III: 20,19 $\rightarrow$ 11,24 (p<0,001) Stage IV: -	Inability to pro- vide intergroup homogeneity in terms of Pres- sure Ulcer Stage and Wound Surface Area because of randomiza- tion. Absence of the control group (Standard Wound Care- SWC) Both methods promise good results in re- ducing the traumatic sur- face and heal- ing pressure ulcers.
2. Polak et	Evaluation	Randomized,	Prognosis for pressure ul-	Patients' char-	Reduction in	Small number

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Poland.	ciency be- tween high frequency ultrasound (HFUS) and electrical stimulation (ES).	Hospitalized patients in 2 types of nurs- ing and care centers— residential care facilities and temporary care facilities (n=77), with pressure ulcers (n=88). Stage II: 60 (68.1%) Stage III: 22 (25.0%) Stage IV: 6 (6.8%) Patient group with Standard Wound Care (SWC) (n=28) Patient group with SWC+US (n=25) Patient group SWC+ES (n=24) Study duration: 3 years.	ton scale, Braden scale, nutritional status with Nutritional Risk Score. Classification of pressure ulcers with NPUAP, EPUAP and PPPIA. <b>SWC</b> : contin- uous ulcer assessment, blood tests, use of wound dressings, mobilization, cleansing of necrotic tis- sues. <b>HFUS</b> : once a day, 5 days a week. <b>ES</b> : once a day, for 50', 5 days a week. Duration of monitoring: 4 and 6 weeks.	for normality of distribution with Shapiro- Wilk W-test. Patient char- acteristics in the 3 groups were evaluat- ed for hetero- geneity using the two-sided Fisher's exact test, the Krus- kal-Wallis test and the Krus- kal-Wallis post-hoc test. Mean WSA before and after treat- ment were compared using the Wil- coxon signed- rank test. The level of significance was set at p<0.05.	(cm <sup>2</sup> ): SWC + US group: 10,86→3,69 SWC + ES group: 7,48→2,65 SWC group: 9,31→5,33 (p<0.0001). The percent- age reduction in the surface area of Pus (4 weeks): SWC + US group: 70,93% SWC + US group: 68.3% SWC group: 39% The percent- age reduction in the surface area of PUs (6 weeks): SWC + US group: 77.48% SWC + US group: 77.48% SWC + US group: 77.48% SWC + ES group: 76,19% SWC group: 48,97% Healing in 6 weeks: SWC + US group: 13/28 (46,43%) SWC + ES group: 15/29 (51,72%) SWC group: 7/31 (22,6%)	duration of the research. Patients were not blinded, control groups with sham ES and sham US were not creat- ed. The healing ulcers were significant in all three groups, but pressure ulcers de- creased signifi- cantly more and faster with the two consid- ered methods.
<b>3.</b> Polak et al., 2014, Poland.	Evaluation and compar- ison of HFUS efficacy in stage II and III pressure ulcers in combination with stand- ard wound	Prospective, randomized, controlled clini- cal study. Elderly patients admitted to 4 centers (n=42), with PrUs (n=44).	Prognosis for pressure ul- cers with Nor- ton scale and Braden scale, nutritional status with Nutritional Risk Score.	Statistical analysis: StatSoft Pol- ska Sp. z o.o. version 8.0. Patient char- acteristics: Shapiro-Wilk W-test.	Total average reduction in the surface area of PrUs (cm <sup>2</sup> ): SWC + HFUS group: 15,38→6,16 (p=0,000069) SWC group:	The study lacked patient blinding and the non- application of sham HFUS to the control group. Probably dif-

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care (SWC)		Classification		11,08→8,28	ferent SWC due
versus	Stage II: 32	of pressure	Distribution	(p=0,0062)	to 4 research
standard	(72.73%)	ulcers with	homogeneity		centers.
wound care	Stage III: 12	NPUAP and	of patient	The percent-	
only.	(27.27%)	EPUAP.	characteristics	age reduction	Ulcers in the
,	· · · ·		in both	in the surface	SWC + HFUS
	SWC group:	SWC: regular-	groups: Fisher	area of Pus (6	group de-
	(n=22) with	ly assessment	test και	weeks):	creased more
	PrUs (n=23),	of wounds,	Mann-	SWC + HFUS	in size.
	Stage II: 18 and	blood analy-	Whitney U	group: 68.80%	
	Stage III: 5.	sis, use of	test.	SWC group:	The weekly
	Stage III. 5.	wound dress-	lest.	37.24%	healing rate of
	SWC+HFUS		The level of	(p=0,047)	ulcers in the
		ings, mobili-			SWC + HFUS
	group (n=20)	zation, cleans-	significance	Weekly aver-	group was bet-
	with PrUs	ing of necrotic	was set at	age reduction	ter than in ul-
	(n=21), Stage II:	tissues.	p≤0.05.	in the surface	cers in the SWC
	14 and Stage			area of PrUs	group, but not
	III: 7.	HFUS: once a		(cm <sup>2</sup> ):	statistically
		day, 5 days in		SWC +HFUS	significant. On-
	Study duration:	a week.		group: 2.63	ly for ulcers
	2,5 years.			SWC group:	Stage II it was
		The healing		1.52	statistically
		progress of		(p = 0,07)	significant.
		ulcers receiv-		(p = 0,01)	Significant.
		ing SWC and		Stage II SWC +	More stage II
		SWC+HFUS		HFUS: 3,09	ulcers of the
		was moni-		Stage II SWC:	SWC + HFUS
		tored for 6		1,08	group were
		weeks or until		(p=0,045)	reduced to the
		wounds			surface by at
		closed.		Stage III SWC +	least 50% com-
				HFUS: 1,70	pared to the
				Stage III SWC:	same ulcers of
				3,44	the SWC group.
				(p=0,65)	the swc group.
				Healing in 6	
				weeks:	
				SWC + HFUS	
				group: 8/21	
				(38,09%) (p =	
				0.062)	
				SWC group:	
				3/23 (13,04%)	
				(p = 0.999)	
				Stage II SWC +	
				HFUS 50%:	
				11/14	
				Stage II SWC	
				50%: 7/18	
				(p=0,035)	
				(,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,	
				Stage III SWC +	
				HFUS 50%: 4/7	

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					50%: 3/5 (p=0,999)	
4.	Investigation	Pilot random-	Classification	At each dress-	(p=0,999) Treatment	Small sample
 Maeshige	and evalua-	ized controlled	of pressure	ing change,	group (US):	size.
et al.,	tion of the	clinical trial.	ulcers with	the wound	Wound size: In	0.201
2010,	effect of		NPUAP.	size and exu-	ulcers 1 and 2,	The efficacy of
Japan.	ultrasound in	Elderly neuro-		date weight	a marked re-	US in the
	combination	logical patients	Application of	were meas-	duction in	treatment of
	with stand-	(n=5), with	US for 10', 5	ured.	wound size was	PrUs is not cer-
	ard wound	PrUs Stage III	days per week		observed after	tain.
	care with a	and IV (n=7).	for 2-4 weeks.	The <b>DESIGN</b>	3–4 weeks of	
	wound			(P) classifica-	US treatment.	It seemed that
	dressing in	PrUs without	All patients	tion	In ulcer 3, a	the delivered
	the treat-	local wound	received	scale was used	reduction was	intensity of US
	ment of	infection and	standard	to evaluate	observed as	0,5W/cm <sup>2</sup> can
	pressure	extensive ne-	wound care	the total char-	soon as US	penetrate per-
	ulcers.	crotic tissue.	throughout	acteristics	treatment be-	meable dress-
		Patients with-	the study.	of each PrUs:	gan. In ulcer 4,	ings that keep
		out diabetes		<ul> <li>Depth</li> </ul>	no clear reduc-	the wound
		mellitus type 2	Period A:	<ul> <li>Exudate</li> </ul>	tion was seen.	moist and had
		and/or periph-	Each ulcer	• Size	Exudate	a positive effect
		eral arterial	received	<ul> <li>Infection</li> </ul>	weight: In	on healing.
		disease.	standard	Granulation	ulcers 1 and 2,	
			wound care	Necrosis	exudates	The implemen-
		Treatment	only for 2–4	<ul> <li>Pocket</li> </ul>	weight in-	tation of the US
		group (US): 3	weeks.		creased during	in conjunction
		patients with 4		Wound size:	US therapy. In	with the stand-
		ulcers (ulcers 1-	Period B:	A pen-tablet	ulcer 3, there	ard wound care
		4).	standard	system (Intuos	was no such	could promote
		Control group	wound care +	3, Wacom,	increase. In	the healing of
		(sham US): 2	US or sham US for 2-4	Japan) was used to meas-	ulcer 4, exudate weight could	pressure ulcers.
		patients with 3 ulcers (ulcers 5-	weeks in an	used to meas- ure the	not be meas-	
		7).	ABABA se-	wound. The	ured as it	
		7).	quence.	wound shape	leaked from the	
		One ulcer was	quence.	was digitized	dressing.	
		not random-	The ulcers	and the area	uressing.	
		ized, but was	were random-	measured	Control group	
		the first to re-	ly assigned	using Scion	(sham US):	
		ceive in the	(via a toss of a	Image soft-	Wound size:	
		BABA se-	coin) to the	ware.	These ulcers	
		quence, with a	US group or		showed no	
		view to deter-	the control	Exudate	marked reduc-	
		mining if the	group. The	weight: This	tion in wound	
		pilot was feasi-	latter group	was measured	size. One ulcer	
		ble.	received sham	by subtracting	(ulcer 6) was	
			US at period	the weight of	withdrawn from	
			В.	the dressing	the study after	
				before appli-	it increased in	
				cation from	size.	
				the weight	Exudate	
				immediately	weight: In ul-	
				after removal.	cers 5–7, exu-	
					date weight	
				Any dressings	was dependent	

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				that were soaked with urine were excluded from the analysis.	on wound size, no increase in weight was recorded.	
5. Serena et al., 2009, H.П.А.	Evaluation of the effec- tiveness of non-touch low frequen- cy ultra- sound ther- apy (MIST Therapy) in reducing bacterial colonization in stage III pressure ulcers and promoting healing.	Prospective experimental study. Patients with musculoskeletal disorders (mean age: 60 years) in 3 trauma care centers (n = 11). Chronic stage III pressure ulcers with a wound volume of up to 160 cm3 and bacte- rial measure- ments > 105 CFU/g of tissue (without infec- tion) were studied. (Colony Form- ing Units per gram of tissue: CFU/g of tis- sue) Patients with- out clinical symptoms of acute ulcer infection, with- out head or neck injury, without malig- nancy in the wound bed.	Assessment of the bacterial load of the ulcer by quantitative tissue biopsy before and 2 weeks after MIST Thera- py: 3 times per week for 2 weeks. Average du- ration of each treat- ment: 4' All patients underwent the standard wound care (SWC) during the study. (SWC: appro- priate sup- portive sur- face, pressure relief, nutri- tional status control and dressings exudates management). Systemic and local antibiot- ics, local anti- septics, EMLA cream, anti- microbial dressings were not al- lowed.	Descriptive statistics were performed to summarize and compare the baseline data with re- sults after 2 weeks of MIST Therapy. Bacterial quantities were summa- rized in CFU/g tissue.	The bacterial load was re- duced from 4x107 to $2x107after MISTTherapy.A different re-sponse ofGram- andGram+ bacteriato ultrasoundtherapy wasobserved.The Staphylo-coccus species,including MRSA(Staphylococcusaureus resistantto methicillin)were signifi-cantly reducedafter treatment.However, Strep-tococcus Gshowed only amoderate de-crease and thenumber ofStreptococci Aincreased in anindividual.Healing in 2weeks:The ulcer sur-face was re-duced by 26%(13,8cm2 \rightarrow10,8 cm2) andthe ulcer vol-ume was re-duced by 20%(18,5cm3 \rightarrow11,6cm3).$	Absence of the control group. The non-touch low frequency ultrasound (LFUS) treat- ment reduces the bacterial load in the ul- cer bed pro- moting the healing.