

Therapie der kutanen Leishmaniasis

Thermotherapie



Auswärtiges Amt

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Gemeinschaftsprojekt



Deutsche Gesellschaft für
Tropenmedizin und
Internationale Gesundheit

Paul-Ehrlich-
Gesellschaft für
Chemotherapie



„Kutane/mukokutane Leishmaniasis*“

- AWMF Leitlinie Nr. 042/007 -

<http://www.uni-duesseldorf.de/AWMF/II/042-007.htm>

erstellt durch AG Leishmaniasis



**Society for Dermatology
in the Tropics**

**AG Dermatologische
Infektiologie der DDG**



* Boecken, G., Weitzel, T., Sunderkotter, C., Fischer, M., von Stebut-Borschitz, E., Bogdan, C., Pietras, M., Anders, G., Harms-Zwingenberger, G., Burchard, G., Bialek, R., Lippert, U., Grobusch, M., Erkens, K., Fleischer, B., Lobermann, M., Schunk, M., Sterzik, B., **Diagnosis and therapy of cutaneous and musculoskeletal Leishmaniasis in Germany**, J Dtsch Dermatol Ges 2009, 7 Suppl 7, s1-38

WHO Technical report series 949 – 2010

Therapie der kutanen Leishmaniasis – Neue Welt (NWCL)

Local therapy was considered unsuitable for the treatment of New World cutaneous leishmaniasis caused by *L. braziliensis* or *L. panamensis* because of the potential risk of metastasis; however, as systemic treatment does not guarantee prevention of later mucocutaneous leishmaniasis, which is found in < 5% of the cases, local treatments should be explored. It is now considered acceptable to use topical therapy in selected cases of New World cutaneous leishmaniasis.

- WHO 2010: Paradigmenwechsel in der Therapie der NWCL
⇒ lokale Therapie als Option gegeben, da
 - MCL nur in < 5% der Fälle
 - systemische Therapie keine Garantie für Prävention der MCL ist

WHO Technical report series 949 – 2010

Therapie der kutanen Leishmaniasis – Neue Welt (NWCL)

The options proposed are thermotherapy and paromomycin. One to three applications of localized heat (50 °C for 30 s) were about 70% effective in Colombia and Guatemala 3 months after treatment (A) Paromomycin at 15% plus methyl benzethonium chloride 12% ointment twice daily for 20 days was 70–90% effective against cutaneous leishmaniasis caused by *L. mexicana*, *L. panamensis* and *L. braziliensis* in Ecuador and Guatemala (B).

Optionen:

- Thermotherapie
- Paromomycin-Salbe

Thermotherapie

"Wer Krankheit nicht mit Medizin heilen kann, soll operieren. Was er nicht operieren kann, soll er mit Wärme heilen. Wer mit Wärme nicht zu heilen ist, dem ist nicht zu helfen.", Hippokrates (460-370)

Malariafiebertherapie war vor der Antibiotika-Ära die einzige wirksame Therapie bei progressiver Paralyse, dem Spätstadium der Syphilis.

Dr. Wagner von Jauregg erhielt 1927 den Medizin-Nobelpreis für seine damals gewagte Fiebertherapie

Thermosensitivität von Leishmanien

Pereira, C., Castro, P. de, and Mello, D. de, 1958.
Influencia da temperatura cutanea no desenvolvimento de lesões leishmanioticas. *Arq. Inst. Biol. (S. Paulo)*, 25: 121–138.

EFFECTO DE LA TEMPERATURA DE LA PIEL EN LA LEISHMANIASIS CUTANEA EXPERIMENTAL *

Maio-Jun., 1971

Rev. Soc. Bras. Med. Trop.

133

kutane Läsionen bei Tieren und Menschen konnten mit Wärme zur Abheilung gebracht werden (Pereira et al. (1958), Zeledon et al. (1971))

350

THE NEW ENGLAND JOURNAL OF MEDICINE

Feb. 15, 1979

MEDICAL INTELLIGENCE



CURRENT CONCEPTS IN PARASITOLOGY

Leishmaniasis

Philip D. Marsden, M.D.

has to be used. Diffuse cutaneous leishmaniasis is difficult to treat, but some success has been achieved with immersion in hot water twice daily. Heat therapy deserves further evaluation for cutaneous lesions. If

Thermosensitivität von Leishmanien

Am. J. Trop. Med. Hyg., 30(2), 1981, pp. 318–321
Copyright © 1981 by The American Society of Tropical Medicine and Hygiene

EFFECT OF TEMPERATURE ON MULTIPLICATION OF *LEISHMANIA* AMASTIGOTES WITHIN HUMAN MONOCYTE-DERIVED MACROPHAGES IN VITRO

JONATHAN D. BERMAN AND FRANKLIN A. NEVA

*Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases,
National Institutes of Health, Bethesda, Maryland 20205*

Abstract. *Leishmania tropica*, a cause of cutaneous leishmaniasis, multiplied more rapidly within human macrophages in vitro at 35°C than at 37°C, and was almost completely eliminated at 39°C. In contrast, *Leishmania donovani*, the cause of the visceral leishmaniasis, multiplied equally well at 35°C and at 37°C, and was only 40% eliminated at 39°C. This in vitro study suggests that the localization of the two strains to cooler and warmer regions of the body, respectively, is at least partially explained by the inherent temperature sensitivity of the parasite-macrophage unit. The striking elimination of this strain of *L. tropica* within macrophages at 39°C may make this model suitable for predicting the clinical response of cutaneous strains to heat therapy.

1981 – Berman u. Neva:

⇒ *L. tropica* Vermehrung in Makrophagen in vitro stärker bei 35° als bei 37°; bei 39° kein Wachstum mehr

⇒ *L. donovani* (VL-Erreger) wächst weiter auch bei 39°



Thermosensitivität von Leishmanien

Am. J. Trop. Med. Hyg., 32(2), 1983, pp. 300–304

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THERMOSENSITIVITY PATTERNS OF OLD VS. NEW WORLD CUTANEOUS STRAINS OF *LEISHMANIA* GROWING WITHIN MOUSE PERITONEAL MACROPHAGES IN VITRO*

DAVID L. SACKS, ALDINA BARRAL, AND FRANKLIN A. NEVA

*Laboratory of Parasitic Diseases, National Institute of Allergies and Infectious
Diseases, National Institutes of Health, Bethesda, Maryland 20205*

Abstract. Infection of mouse peritoneal macrophages in vitro was used to examine the effect of elevated temperature on the intracellular replication of various strains of *Leishmania*. Of eight cutaneous strains examined, all grew optimally at 35°C. At 37°C the reduction in growth was most pronounced for the New World cutaneous strains, and at 39°C three of four New World cutaneous strains were completely destroyed whereas all of the *L. tropica* strains survived and exhibited at least 100% growth after 3 days. The results of these in vitro studies correlate closely with the outcome of heat therapy on two patients with cutaneous disease, suggesting that, in general, cutaneous lesions due to *L. tropica* strains might be less responsive to heat therapy than lesions due to *L. mexicana* and related strains.

1983 – Sacks, Barral, Neva:

Temperaturempfindlichkeit von 8 Leishmanienspezies (OWCL und NWCL) in Makrophagen getestet.

⇒ alle hatten bei 35° ihr Wachstumsoptimum

⇒ bei 37° wuchsen die NWCL schlechter als die OWCL-Stämme

⇒ bei 39° überlebten nur *L. tropica* und *L. donovani* – anders als Berman 1981

⇒ Erklärung: unterschiedliche Kulturmedien (Makrophagenzellschicht # Suspension)



Thermotherapie von Leishmanien Infrarot

September 1986, Vol. 25, No. 7

Pharmacology and Therapeutics

Treatment of Cutaneous Leishmaniasis with Infrared Heat

ABDUL JABBAR N. JUNAID, M.D.

472

INTERNATIONAL JOURNAL OF DERMATOLOGY September 1986

Vol. 25

1986 Junaid :

- 178 Patienten mit *L. tropica*, bestrahlt mit Hitzequelle 55° für 5 Min
- Wiederholung bei 16 Patienten nach 3 Wochen
⇒ Abheilung aller Läsionen nach 6 Wochen.
- Beobachtung: Therapie einer Läsion läßt alle anderen Abheilen
- keine Kontrollgruppe, kein Langzeit-follow-up

Thermotherapie von Leishmanien

Ultraschall

Ultrasound-Induced Hyperthermia in the Treatment of Cutaneous CUTIS Leishmaniasis

VOLUME 40, OCTOBER 1987 353

Homayoon Aram, MD, Jerusalem, Israel
Vera Leibovici, MD, Jerusalem, Israel

1987 Aram et al.:

- 18 Patienten mit 28 Läsionen *L. major* in Lokalanästhesie
- 42° für 3 min, 2-3mal/Woche 10-15 mal, Temperaturkontrolle über Sonde
- Heilungsrate nach 5-10 Wochen:
 - ⇒ 22 Läsionen bei 13 Patienten (78,5%) abgeheilt
- keine Kontrollgruppe, kein Langzeit-follow-up

Thermotherapie - Radiowellen (RF)

- ✓ Eindringtiefe der Radiowellen einheitlich 4 mm,
⇒ Schutz der tiefen Hautschichten
- ✓ FDA hat thermochirurgische Apparatur zur Therapie der CL zugelassen
 - ⇒ leicht zu bedienen
 - ⇒ Einstellung und Kontrolle der applizierten Temperatur gut möglich
 - ⇒ Selbstregulierung der Temperatur
 - ⇒ leichtes Gewicht, batteriebetrieben, feldtauglich



<http://www.thermosurgery.com/>

Thermotherapie – Radiowellen (RF)

PLACEBO-CONTROLLED CLINICAL TRIAL OF MEGGLUMINE ANTIMONATE (GLUCANTIME) VS. LOCALIZED CONTROLLED HEAT IN THE TREATMENT OF CUTANEOUS LEISHMANIASIS IN GUATEMALA

THOMAS R. NAVIN, BYRON A. ARANA, FLORA E. ARANA,
ANA MARÍA DE MÉRIDA, A. LORENA CASTILLO,
AND JULIO L. POZUELOS

*Medical Entomology Research and Training Unit/Guatemala, Division of Parasitic Diseases,
Center for Infectious Diseases, Centers for Disease Control, Atlanta, Georgia; and Sanidad
Militar, Guatemala City, Guatemala*

Abstract Sixty-six Guatemalans with parasitologically proven cutaneous leishmaniasis were randomly and equally divided into 3 treatment groups: those receiving meglumine antimonate (Glucantime), 850 mg antimony/day im for 15 days; those receiving localized controlled heat from a radio-frequency generator, 50°C for 30 sec, 3 treatments at 7 day intervals; and those receiving treatment with a placebo. Of 53 isolates identified, 40 were *Leishmania braziliensis braziliensis* and 13 were *L. mexicana mexicana*. Thirteen weeks after beginning treatment, the number of patients from each group with completely healed and parasitologically negative lesions were as follows: meglumine antimonate, 16 (73%); localized heat, 16 (73%); and placebo, 6 (27%). The cure rate for those with infections due to *L. b. braziliensis* in each group was as follows: meglumine antimonate, 11 out of 14 (79%); controlled heat, 9 out of 14 (64%); and placebo, 0 out of 11.



1990 Navin et al.

- Erste Placebo-RCT: RFHT 50° für 30 Sek., 3x im Abstand von 7 d $\Rightarrow$ 6 x 4 cm Erythem vs. Antimon 10-20mg/Kg KG i.m. für 15 d vs. Placebo-Radiowellen
- RF-Generator Thermosurgery®, 6,78 mHz, Temperaturwahlschalter, Temp.-Kontroll-Sonde
- superinfizierte Ulzera vorher antibiotisch therapiert, Lokalanästhesie + Adrenalin
- 25% *L. mexicana*, 75% *L. braziliensis*, bis 52 Wochen follow up

Thermotherapie - Radiowellen

- Heilungsraten nach 13 Wochen insgesamt:
 - ⇒ 73 % je mit Antimon und RFHT
 - ⇒ 27 % mit Placebo-Radiowellen
- Bei *L. braziliensis*:
 - ⇒ 79% mit Antimon
 - ⇒ 64 % RFHT
 - ⇒ Placebo 0%
- langsamere Ansprechrate bei RFHT
- keine Mitbehandlung unerkannter Läsionen
- jedoch bei follow-up von 600 Patienten über 12 Monate keine MCL

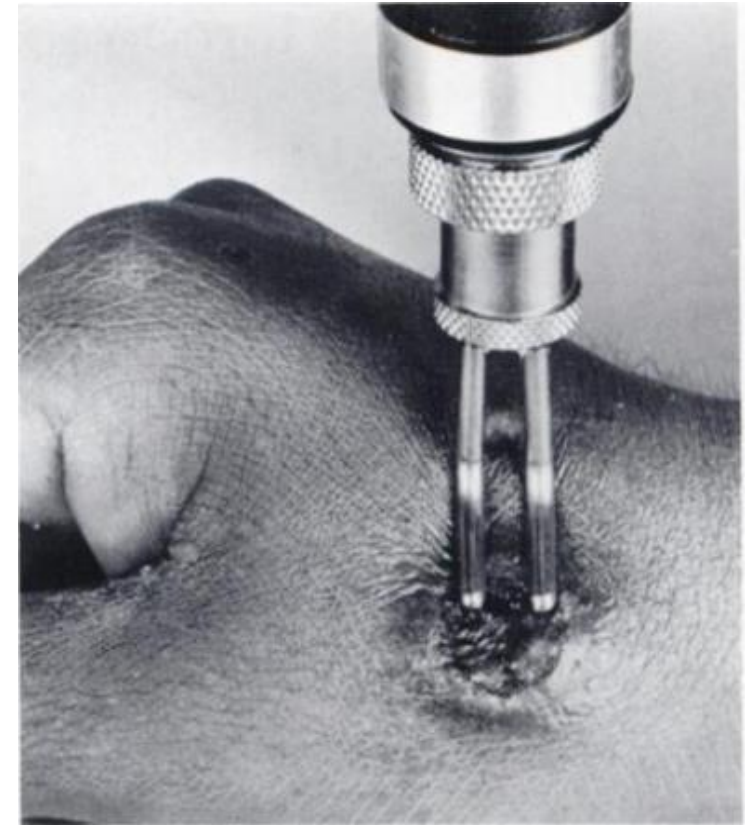


FIGURE 1. A wand that consists of 2 electrodes extends from the heat apparatus. If the lesion was larger than the area covered by the 2 electrodes, multiple 30 sec treatments were applied.



Thermotherapie - Radiowellen

Am. J. Trop. Med. Hyg., 57(3), 1997, pp. 309–312

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TREATMENT OF CUTANEOUS LEISHMANIASIS WITH LOCALIZED CURRENT FIELD (RADIO FREQUENCY) IN TABASCO, MEXICO

O. VELASCO-CASTREJON, B. C. WALTON, B. RIVAS-SANCHEZ, M. F. GARCIA, G. J. LAZARO, O. HOBART,
S. ROLDAN, J. FLORIANI-VERDUGO, A. MUNGUIA-SALDANA, AND R. BERZALUCE

*Instituto Nacional de Diagnostico y Referencia Epidemiologica, Colonia Santo Tomas, Mexico DF; Gettysburg, Pennsylvania;
Secretaria de Salud del Estado de Tabasco e Hospital General de Comalcalco, Tabasco, Mexico*

1997 Velasco-Castrejon et al.

- 201 Patienten mit *L. mexicana* („Chiclero Ulcer“)- **Machbarkeitsstudie**
- LA und Wundreinigung, dann RFHT 50° für 30 Sek.
 - ⇒ nach 4 Wochen 122/201 zu 95% abgeheilt
 - ⇒ nach 8 Wochen 191/201 zu 90% abgeheilt
- keine Kontrollen, aber
 - ⇒ Selbstheilung bei *L. mexicana* ist entgegen der Lehrmeinung nicht hoch, insbesondere nicht bei Knorpelbeteiligung

Gutes Verfahren für die Feldbehandlung vieler Patienten, insbesondere bei Knorpelbeteiligung

Chiclero-Ulzera





Thermotherapie - Radiowellen

MAJOR ARTICLE

EDITORIAL COMMENTARY

Efficacy of Thermotherapy to Treat Cutaneous Leishmaniasis Caused by *Leishmania tropica* in Kabul, Afghanistan: A Randomized, Controlled Trial

R. Reithinger,^{1,4} M. Mohsen,¹ M. Wahid,² M. Bismullah,² R. J. Quinnell,³ C. R. Davies,⁴ J. Kolaczinski,^{1,4} and J. R. David⁵

¹Malaria and Leishmaniasis Control Program, HealthNet International, University Town, Peshawar, Pakistan; ²Afghan Ministry of Health, Kabul, Afghanistan; ³School of Biology, University of Leeds, Leeds, and ⁴Department of Infectious and Tropical Diseases, London School of Hygiene & Tropical Medicine, London, United Kingdom; and ⁵Department of Immunology and Infectious Diseases, Harvard School of Public Health, Boston, Massachusetts

(See the editorial commentary by Wortmann on pages 1156–8)

Boiling the Boil

Glenn Wortmann

Infectious Disease Service, Walter Reed Army Medical Center, Washington, D.C., and Uniformed Services University of the Health Sciences, Bethesda, Maryland

(See the article by Reithinger et al. on pages 1148–55)

2005 Reithinger et al.

- RCT, *L. tropica*, Kabul, 401 Patienten, Einzelläsion,
- RFHT 50° für 30 Sek. vs. pl-Antimon vs. i.m.-Antimon
 - ⇒ Abheilung nach 100 Tagen: 69,4% RFHT, 75,3% plA, 44,8% i.m. AM
 - ⇒ schnellere Abheilung unter RFHT

Schlußfolgerung: Einsatz der RFHT hängt ab von:

- klinischen Faktoren wie Ort, Größe und Anzahl der Läsionen,
- Management der Infektion wie Möglichkeiten des Follow-ups, Behandlungszeit

Limitationen:

- Nebenwirkungen, Blasenbildung, Infektion, Hypopigmentierung, Narbenbildung größer
- Kontrollgruppe i.m. AM war unterdosierte, nur kleine und Einzelläsionen behandelt

Thermotherapie - Radiowellen

Transactions of the Royal Society of Tropical Medicine and Hygiene (2006) 100, 642–649



available at www.sciencedirect.com

SCIENCE @ DIRECT®

journal homepage: www.elsevierhealth.com/journals/trst



2005 Lobo et al.

- *L. braziliensis*
- 37 Pat. 17x RFHT, 20x Antimon, 28 d follow-up
- RFHT Pat. - AM Nachbehandlung
⇒ Heilungsprozess initiiert bei 75% RFHT, 90% AM
⇒ Heilung auch nicht behandelter Läsionen nach RFHT ⇒
⇒ systemischer Effekt auch durch RFHT bestätigt

Heat therapy for cutaneous leishmaniasis elicits a systemic cytokine response similar to that of antimonial (Glucantime) therapy

Iza M.F. Lobo^a, Milena B.P. Soares^b, Tania M. Correia^b, Luiz A.R. de Freitas^b, Maria Ines Oliveira^a, Maria Nakatani^a, Eduardo Netto^a, Roberto Badaro^a, John R. David^{c,*}



Thermotherapie - Radiowellen

Clinical dermatology • Original article

doi: 10.1111/j.1365-2230.2007.02405.x

Efficacy of local heat therapy by radiofrequency in the treatment of cutaneous leishmaniasis, compared with intralesional injection of meglumine antimoniate

© 2007 The Author(s)

Journal compilation © 2007 Blackwell Publishing Ltd • *Clinical and Experimental Dermatology*, **32**, 371–374

G. Sadeghian, M. A. Nilfroushzadeh and F. Iraj*

*Skin Disease and Leishmaniasis Research Center, Isfahan University of Medical Sciences and Health Services, Isfahan, Iran; and *Isfahan University of Medical Sciences and Health Services, Isfahan, Iran*

2007 Sadeghian et al.

- RCT mit 117 Pat., *L. tropica*,
- RFHT 50° für 30 sec vs. plA 1x wöchtl. für 4 Wo, 6 Monate follow-up
 - ⇒ Heilungsrate 80,7% mit RFHT, 55,3% mit plA, kein Relaps
 - ⇒ geringere Narbenbildung unter RFHT
 - ⇒ schnellere Heilung unter RFHT



Thermotherapie - Radiowellen

Transactions of the Royal Society of Tropical Medicine and Hygiene (2009) 103, 703–706



available at www.sciencedirect.com



journal homepage: www.elsevierhealth.com/journals/trst



The efficacy of thermotherapy to treat cutaneous leishmaniasis in Colombia: a comparative observational study in an operational setting

Juan Carlos Vega^{a,b}, Boris Fernando Sanchez^c, Luz Mery Montero^c, Rafael Montaña^c, Mercedes del Pilar Mahecha^c, Bladimir Dueñez^c, Ángela Rocío Baron^c, Richard Reithinger^{d,e,*}

2009 Vega et al.

- Unverblindete Beobachtungsstudie, *L. guyanensis* (95%), *L. panamensis* (5%)
- 47 Pat. RFHT 50° für 30 sec vs. 60 Pat. i.m. AM 20mg/kg/KG für 21 d,
- 1, 2 und 3 Monate follow-up
 - ⇒ Heilungsraten nach 3 Monaten: 38% mit RFHT vs. 42% AM
 - ⇒ Feldstudie, schlechter Follow-up, kleine Fallzahlen
 - ⇒ aber: im Ausbruch kosteneffektiv, schnell durchführbar, nur 1 Behandlung

A Randomized Controlled Trial of Local Heat Therapy Versus Intravenous Sodium Stibogluconate for the Treatment of Cutaneous *Leishmania major* Infection

Naomi E. Aronson^{1,2*}, Glenn W. Wortmann^{1,2}, William R. Byrne², Robin S. Howard³, Wendy B. Bernstein^{1,4}, Mary A. Marovich^{1,4}, Mark E. Polhemus^{1,2}, In-Kyu Yoon⁵, Kelly A. Hummer^{2,6}, Robert A. Gasser, Jr.^{1,2}, Charles N. Oster^{1,2}, Paul M. Benson²

Conclusions/Significance: Skin lesions due to *L. major* treated with heat delivered by the ThermoMed device healed at a similar rate and with less associated systemic toxicity than lesions treated with intravenous SSG.

Clinical Trial Registration: ClinicalTrials.gov NCT 00884377

2010 Aronson et al.

- RCT, *L. major*
- 27 Pat. RFHT 50° für 30 Sek. vs. 27 Pat. AM i.v. 20mg/Kg für 10 d
- Follow-up 2 und 12 Monate
⇒ Heilungsrate nach 2 Monaten: 73% RFHT / 59% AM - statistisch gleich

Thermotherapie - Radiowellen

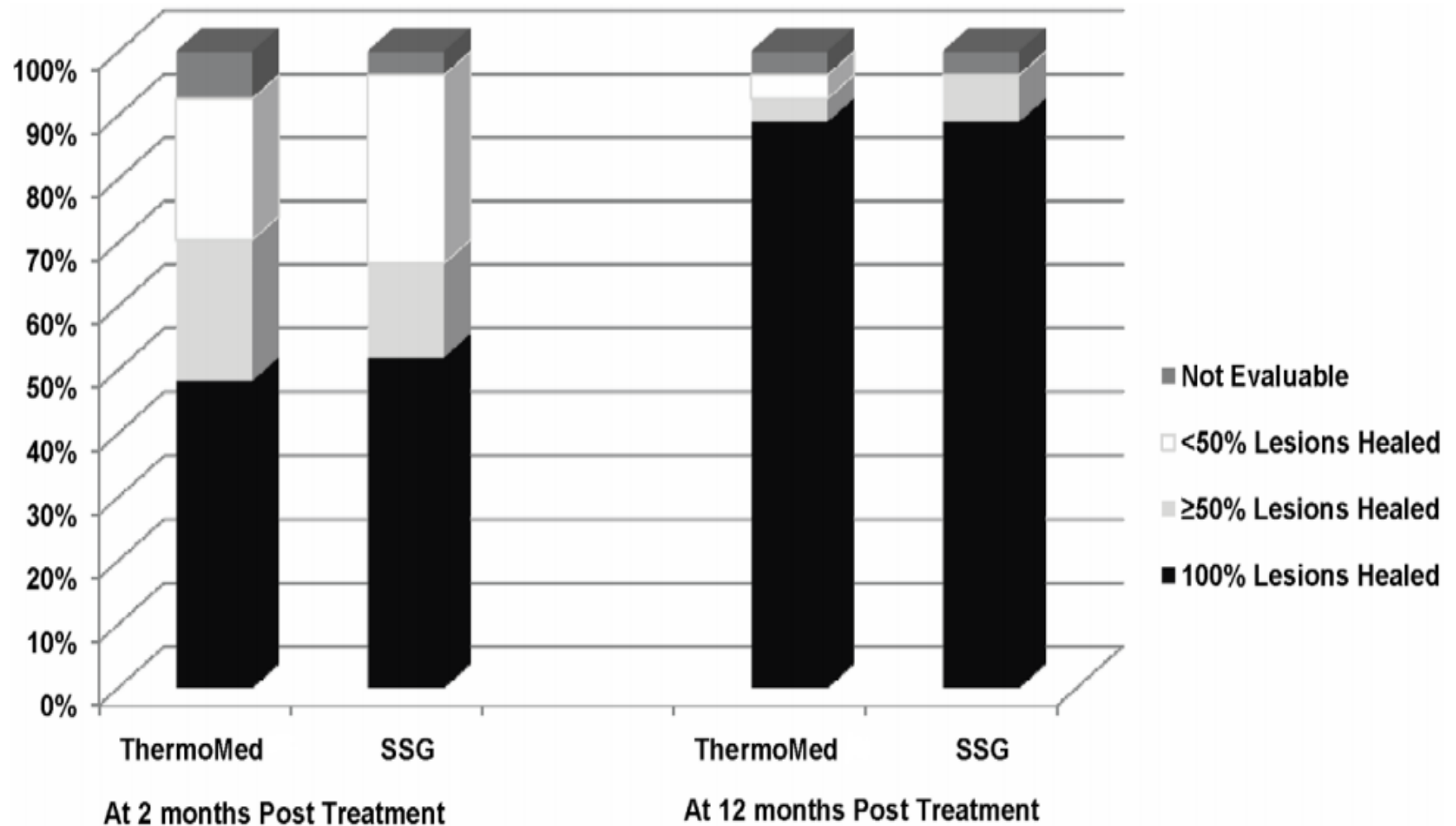


Figure 3. Consensus treatment efficacy at two and twelve months follow-up.

doi:10.1371/journal.pntd.0000628.g003

Thermotherapie - Radiowellen

MILITARY MEDICINE, 177, 3:345, 2012

Evaluation of Thermotherapy for the Treatment of Cutaneous Leishmaniasis in Kabul, Afghanistan: A Randomized Controlled Trial

Najibullah Safi, MD; COL Gary D. Davis, MC USA (Ret.)†; Mohammed Nadir, MD‡;
Hamida Hamid, MD§; COL Leon L. Robert, Jr., MS USA||; MAJ Alan J. Case, MS ARNG (Ret.)†*

2012 Safi et al.:

- RCT, *L. tropica*
- 189 Pat. RFHT 50° für 30 Sek. vs. 193 Pat. plA 1x/Woche für 5 Wochen
 - ⇒ Heilungsrate nach 6 Monaten: 82,5% RFHT vs. 74% plA
 - ⇒ Heilungsrate abhängig von
 - Läsionstyp (Papeln > Knoten > Ulkus)
 - Größe (1cm² > 2 cm² > 4cm²)

Thermotherapie - Radiowellen

López et al. *Trials* 2012, **13**:58
<http://www.trialsjournal.com/content/13/1/58>



RESEARCH

Open Access

Thermotherapy. An alternative for the treatment of American cutaneous leishmaniasis.

Liliana López¹, Martha Robayo², Margarita Vargas² and Iván D Vélez^{1*}

2012 Lopez et al.:

- unverblindete RCT, *L. braziliensis/L. panamensis*, 6 Monate follow-up
- 149 Pat. RFHT 50° für 30 Sek. vs. 143 Pat. AM i.m. 20mg/Kg für 20 d
⇒ Heilungsraten: RFHT 64%/58% (pp/itt) vs. AM i.m. 85%/72% (pp/itt)
⇒ weniger UAW unter RFHT, keine Laborkontrollen, nur 1 Sitzung

Thermotherapie - Radiowellen

CONCISE COMMUNICATION

British Journal of Dermatology

Long-term efficacy of single-dose radiofrequency-induced heat therapy vs. intralesional antimonials for cutaneous leishmaniasis in India

R.A. Bumb,¹ N. Prasad,¹ K. Khandelwal,¹ N. Aara,¹ R.D. Mehta,¹ B.C. Ghiya,¹ P. Salotra,² L. Wei,³ S. Peters⁴ and A.R. Satoskar⁴

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British Journal of Dermatology (2013) 168, pp1114–1119

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2013 Bumb et al.:

- RCT, *L. tropica*, 100 Pat., RFHT 30-60 Sek. vs. plA 2x/Woche insg. 7 Inj.
- Intensives follow-up, 15tägig für 4 Mo, dann 5, 6, 9, 12, 18 Monate
 - ⇒ Zeit bis zur Heilung in beiden Gruppen gleich (10-11 Wo)
 - ⇒ Heilungsraten: 3 Mo: RFHT 94% / plA 92%
 - 6 Mo: RFHT 98% / plA 94%
 - kein Rezidiv in 18 Mo
 - ⇒ weniger Narbenbildung und Dyspigmentierung mit RFHT



Thermotherapie - Radiowellen

THERMOTHERAPY EFFECTIVE AND SAFER THAN MILTEFOSINE IN THE TREATMENT OF CUTANEOUS LEISHMANIASIS IN COLOMBIA

2013 Lopez et al.:

- unverblindet RCT, 66% *L.braziliensis*, 33% *L. panamensis*
- 149 Pat. RFHT 50° für 30 Sek. vs. 145 Pat. Miltefosin 3x50 mg für 28 d
- Follow-up 3 und 6 Monate
 - ⇒ keine speziespezifischen Unterschiede bei den Heilungsraten
 - ⇒ keine signifikanten Unterschiede bei den Heilungsraten
 - ⇒ RFHT gleich effektiv bei weniger UAWs und nur 1 Sitzung
 - ⇒ RFHT kosteneffektiv im Vergleich zu Miltefosin (670 US\$)

Efficacy of miltefosine and thermotherapy. Analysis by protocol and by intention to treat

Analysis	Miltefosine		Thermotherapy		p-value*
	Cure / Total	Efficacy (%) CI 95%	Cure / Total	Efficacy (%) CI 95%	
Intention to treat	85/145	59 (50 - 67)	86/149	58 (49 - 66)	0.9
By protocol	85/122	70 (61 - 78)	86/134	64 (55 - 73)	0.4

*Chi square test.

Radio-Frequenz-Hitze-Therapie (RFHT)

THERMAL DOSE EQUIVALENTS Time / Temperature Relationship

52°C	- 7.5 seconds
51°C	- 15 seconds
50°C	-- 30 seconds (most frequently used treatment setting)
49°C	--- 1 minute
48°C	---- 2 minutes
47°C	----- 4 minutes
46°C	----- 8 minutes
45°C	----- 16 minutes
44°C	----- 32 minutes
43°C	----- 64 minutes
42°C	----- 128 minutes



Verfahren	Erreger	Studientyp	Ergebnis
Infrarot 55° 5 Min	<i>L. tropica</i>	Beobachtung	178/178 abgeheilt nach 6 Wochen
Ultraschall 42° 3 Min, 2-3x/Wo 10-15mal	<i>L. major</i>	Beobachtung	78,5 % abgeheilt nach 5-10 Wochen
RFHT 50° 30 Sek. 3x alle 7 d vs. Antimon vs. Placebo	<i>L. mexicana</i> / <i>L. braziliensis</i>	PC-RT	73 % RFHT 73 % Antimon 27 % Placebo
RFHT 50° 30 Sek.	<i>L. mexicana</i>	Beobachtung	191/201 abgeheilt nach 8 Wochen
RFHT 50° 30 Sek. Vs. Antimon i.m. vs. pl Antimon.	<i>L. tropica</i>	RCT	69,4 % RFHT 75,3 % plA 44,8 % Antimon i.m.
RFHT 50° 30 Sek. vs. Antimon i.m.	<i>L. braziliensis</i>	RCT	75% RFHT 90% Antimon
RFHT 50° 30 Sek. vs. plA 1x/Wo f. 4 Wo	<i>L. tropica</i>	RCT	80,7% RFHT 55,3 % plA
RFHT 50° 30 Sek. vs. Antimon i.m.	<i>L. gyanensis</i> (95%) <i>L. panamensis</i>	Beobachtung	38% RFHT 42% Antimon
RFHT 50° 30 Sek. vs. Antimon i.m.	<i>L. major</i>	RCT	73% RFHT 59% Antimon
RFHT 50° 30 Sek. vs. pl Antimon	<i>L. tropica</i>	RCT	83,5 % RFHT 74% plA
RFHT 50° 30 Sek. vs. Antimon i.m.	<i>L. braziliensis</i> / <i>L. panamensis</i>	RCT	64% RFHT 85% Antimon
RFHT 50° 30-60 Sek. vs. pl Antimon	<i>L. tropica</i>	RCT	98% RFHT 94% Antimon
RFHT 50° 30 Sek. vs. Miltefosin	<i>L. braziliensis</i> / <i>L. panamensis</i>	RCT	64% RFHT 70% Miltefosin

Radio-Frequenz-Hitze-Therapie (RFHT)

- Gute Wirksamkeit bei allen Leishmanien-Infektionen (OWCL u. NWCL)
 - Patienten mit Vorerkrankungen behandelbar, wo systemische Therapie nicht möglich ist
 - Schwangere, Stillende und Frauen im gebärfähigen Alter
- 
- zu Beachten bei NWCL: gute Aufklärung für MCL Symptome
 - mehr als 1 Sitzung wahrscheinlich effektiver
 - neue Gerätegeneration erlaubt Temperaturkontrolle und Abgabe einer standardisierten Wärmemenge
- ⇒ besonders auch in Ausbruchssituationen ein geeignetes Therapeutikum

Manual for case management of cutaneous leishmaniasis in the WHO Eastern Mediterranean Region



Annex 4.

Standard operating procedure for thermotherapy

Thermotherapy is an available technique for the treatment of cutaneous leishmaniasis patients by application of local heat at the site of lesion with a portable, battery-operated, localized current field radiofrequency generator (ThermoMed 1.8; Thermo-surgery Technologies).

Indication

- Papule, nodule or ulcer <4 cm.
- Number of lesions <4 cm.
- Location of the lesion should not be close to the eyes, nose or lips.

Method

A single thermotherapy treatment (one or more applications of localized heat of 50°C for 30 seconds, depending on lesion size). The area between the electrodes covers 49–73 mm². Therefore, several thermotherapy applications may be required to cover a lesion.

Procedure

- Disinfect the lesion and 2 cm border of healthy skin around the lesion with antiseptic (e.g. 0.1% chlorine dioxide solution).
- Anaesthetize the lesion with 1% lidocaine HCl.
- Moisturize the lesion with sterile saline solution.
- Apply the heat locally for 30 seconds.
- Apply chlorine dioxide gel to the lesions and then cover them after treatment.

Patient follow-up

To evaluate the outcome of thermotherapy, follow-up after completion of treatment should be scheduled at 14, 30, 45 and 180 days. It will be important to explain to patients that in case the lesion does not improve they should return to the health facility at any time.



Fragen ?

Vielen Dank !