

**Advances in the treatment of Buruli ulcer  
with hyperbaric oxygen therapy  
in the C.D.T.U.B. of Allada, Benin**

**- a pilot study -**

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# study design

- Randomized controlled trial – pilot study
- Enrollment of 29 patients with informed consent
- Patients with one cutaneous lesion and confirmed diagnosis of Buruli ulcer disease
  - Ziehl-Neelsen stain on smear and biopsy
- All patients have been subjected for 58 days to antibiotic therapy: streptomycin + rifampicin (S+R)
- 14 cases treated with S+R (control group)
- 15 cases treated in addition with hyperbaric oxygen therapy (H.O.T.)

# protocol

As B.U. has different clinical and evolutive patterns we tentatively compared similar groups as follows:

- **Clinical group 1:** nodules or plaques even if ulcerated (diameter <5 cm)
- **Clinical group 2:** plaques and ulcerative lesions (diameter >5cm)
- **Clinical group 3:** limphoedematous extensive forms with possible ulceration

→ Surgical excision of necrotic, limphoedematous or ulcerated tissues performed in mean 4 weeks after S+R

→ Skin grafts performed 3-7days after surgery

# HOT scheme

- 28 treatments (cycles/sessions) per patient  
(one HOT session per day, for 5 consecutive days, for 6 weeks)
- the HOT time-period is 40 days
- single treatment time : 75 minutes
  - 2.5 ATA for 35 minutes
  - + air ATA for 5 minutes
  - + 2,5 ATA for 35 minutes
- total days per patient : 28
- total time per patient: 2100 minutes (35 hours)
- total HOT cycles for 15 patients : 420

# follow-up

performed at: 30 - 60 - 90 days (T1-T2-T3)

## CLINICAL SCORES OF IMPROVEMENT

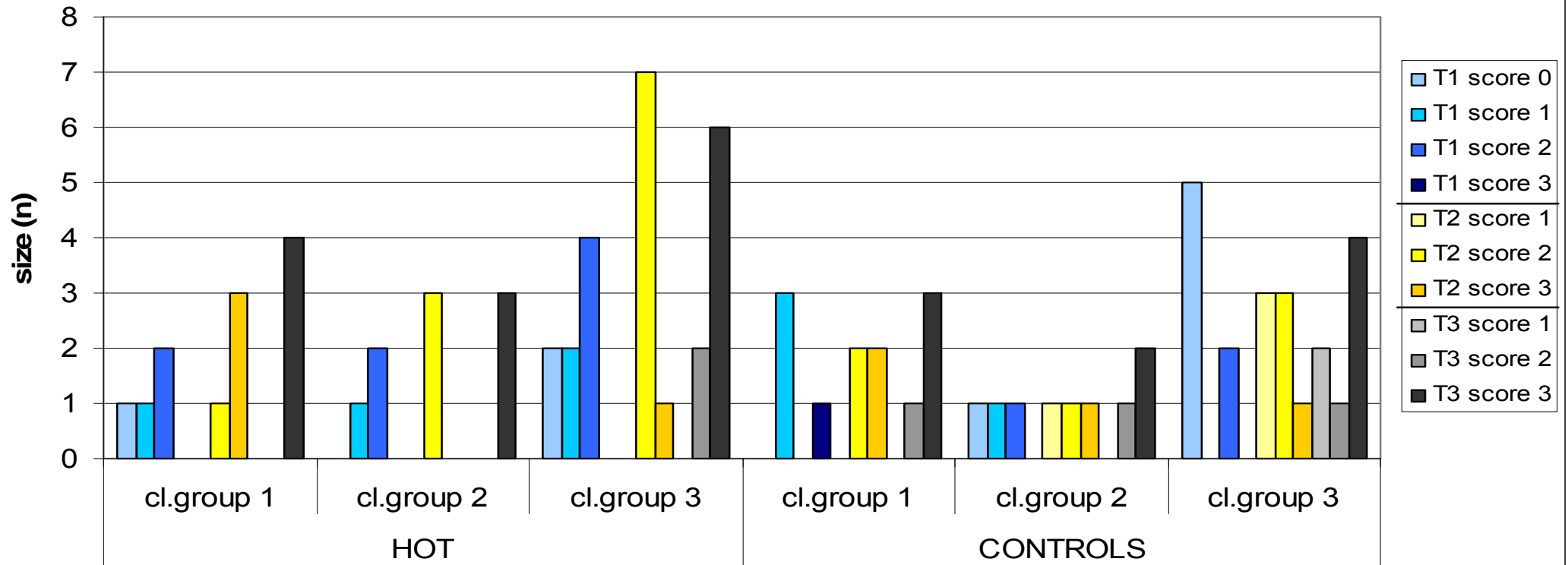
### B.U. OUTCOME EVALUATION

recovered	100%	: score 3
very improved	> 50%	: score 2
improved	< 50%	: score 1
not improved	0%	: score 0

# statistical analysis

- database with data collection and frequencies evaluation of the variables to study
- variance analysis following “One Way Anova”
- Student’s t-test : the single values were evaluated for the groups
- tables reporting the results of the study and statistical significance test are shown

**Clinical score size in HOT (n=15) and Controls (n=14)  
at T1, T2, T3  
in 3 clinical groups**



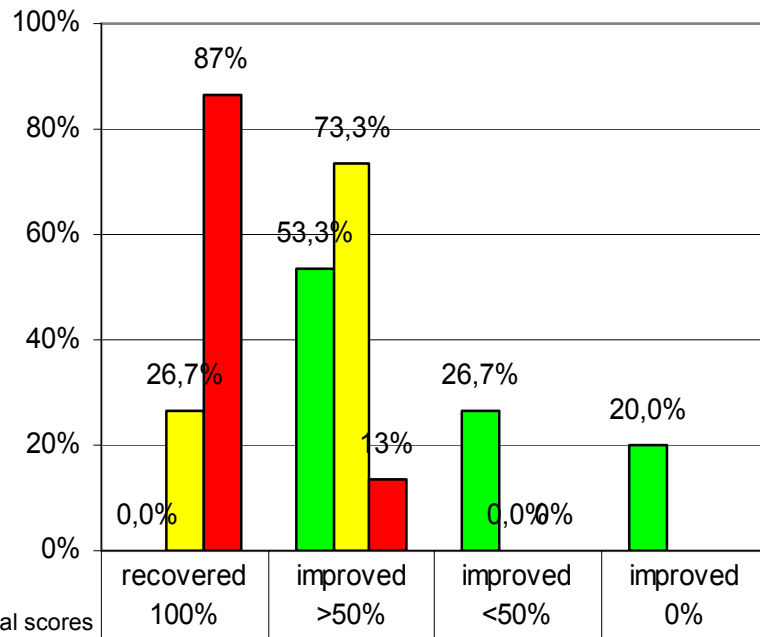
- limited number (size) of total cases (n=29)
- evidence of higher size of improved and cured patients with combined antibiotics plus HOT vs Controls treated only with antibiotics (surgery in all patients when necessary)
- in T2 and T3 the highest scores are in HOT groups, especially in clinical group 2 (very improved) and 3 (recovered)

**Global values of clinical improvement in HOT (n=15) and Controls (n=14)  
at T1, T2, T3  
analysed in function of clinical scores**

		HOT		CONTROLS		TOTAL		single string P value	global P value
		<i>n</i>	%	<i>n</i>	%	<i>n</i>	%		
<b>clinical evaluation at T1</b>	recovered 100%	0	0,0%	1	7,1%	1	3%	0,30	0,15
	improved >50%	8	53,3%	3	21,4%	11	38%	0,08	
	improved <50%	4	26,7%	4	28,6%	8	28%	0,90	
	improved 0%	3	20,0%	6	42,9%	9	31%	0,19	
<b>clinical evaluation at T2</b>	recovered 100%	4	26,7%	4	28,6%	8	28%	0,90	0,26
	improved > 50%	11	73,3%	6	42,9%	17	59%	0,10	
	improved < 50%	0	0,0%	4	28,6%	4	14%	0,03	
<b>clinical evaluation at T3</b>	recovered 100%	13	86,7%	9	64,3%	22	76%	0,17	0,10
	improved > 50%	2	13,3%	3	21,4%	5	17%	0,56	
	improved < 50%	0	0,0%	2	14,3%	2	7%	0,14	
<b>TOTAL</b>		<b>15</b>	<b>100,0%</b>	<b>14</b>	<b>100,0%</b>	<b>29</b>	<b>100%</b>		

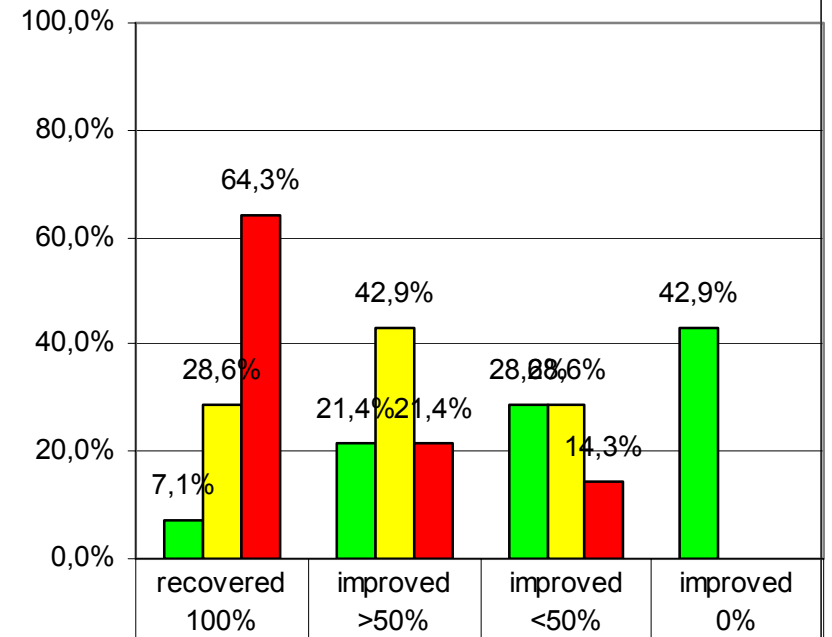
# Global values of clinical improvement in HOT (n=15) and Controls (n=14) at T1, T2, T3 analysed in function of clinical scores

## HOT



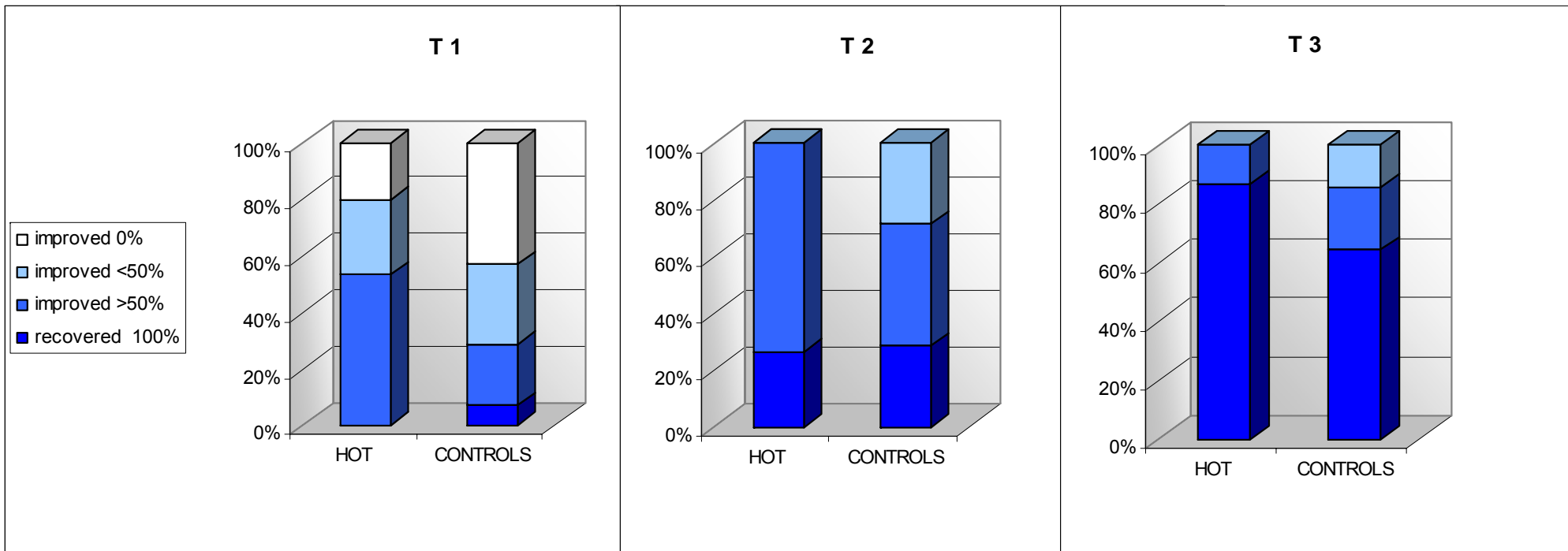
■ clinical evaluation at T1	0,0%	53,3%	26,7%	20,0%
■ clinical evaluation at T2	26,7%	73,3%	0,0%	
■ clinical evaluation at T3	86,7%	13,3%	0,0%	

## CONTROLS



■ clinical evaluation at T1	7,1%	21,4%	28,6%	42,9%
■ clinical evaluation at T2	28,6%	42,9%	28,6%	
■ clinical evaluation at T3	64,3%	21,4%	14,3%	

# Global values of clinical improvement in HOT (n=15) and Controls (n=14) at T1, T2, T3



**t- test**  
**HOT vs CONTROLS**

	Mean HOT	Mean CONTROLS	t value	df	p	N	N	S.D. HOT	S.D. CONTROLS	Variance	p Variance
<b>clinical evaluation at T1</b>	101,73	102,21	-1,45	27	0,15	15	14	0,88	0,89	1,02	0,96
<b>assessment at T1</b>	1,73	2,21	-1,45	27	0,15	15	14	0,88	0,89	1,02	0,96
<b>clinical evaluation at T2</b>	101,73	102,00	-1,12	27	0,26	15	14	0,45	0,78	2,93	0,05
<b>assessment at T2</b>	2,26	2,00	1,12	27	0,26	15	14	0,45	0,78	2,93	0,05
<b>clinical evaluation at T3</b>	101,13	101,50	-1,68	27	0,10	15	14	0,35	0,75	4,65	0,01
<b>assessment at T3</b>	2,86	2,50	1,68	27	0,10	15	14	0,35	0,75	4,65	0,01

# Considerations on the study

- Recent utilization of HOT technique (since May 2005) for BU in West Africa (Benin)
- No side effects have been evaluated on all patients during therapies and at follow-up
- Use of H.O.T. also for other pathologies of common application (osteomyelitis, diabetic foot, vascular or dystrophic chronic ulcers, gaseous gangrene)

# Conclusions (I)

- The number of BU patients, enrolled in this pilot study, treated with HOT (n=15) as well as the number of controls (n=14) is still limited
- Statistical analysis demonstrates, over long periods (T3), the efficacy of HOT with variance  $p < 0.01$  (arbitrarily statistically acceptable for a pilot study)

# Conclusions (II)

- A greater number of patients (sample size study) is necessary for a further evaluation
  - in the near future we plan to continue the study with a RCT in order to reach definitive informations on the efficacy of HOT

## conclusions (III)

- This pilot study confirms also the efficacy of the recommended antibiotic therapy S+R for BU (WHO 2004) : most patients of the control group, only treated with antibiotics, improved or recovered at T2, T3
- We hope that antibiotic therapy in association with HOT, early performed in BU patients, may contribute to reduce the large surgical interventions and to prevent disabilities

# WHO Annual meeting on Buruli ulcer, 15-17/03/2006



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