**Triple Target Treatment (3T) Is More Effective Than Biofeedback Alone for Anal Incontinence: The 3T-AI Study**

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#### ***PURPOSE:*** The efficacy of EMG-biofeedback and low- frequency electrical stimulation for the treatment of anal incontinence has not been proven. Our purpose was to evaluate a novel therapeutic concept, termed triple target treatment, which combines amplitude-modulated medium-frequency stimulation and EMG-biofeedback.

***METHODS:*** Patients with anal incontinence were randomly assigned to the triple target regimen or EMG- biofeedback alone for a 9-month treatment period in a multicenter randomized clinical trial with blinded observers (ClincialTrials.gov registration number NCT00525291). Primary end points were changes in the Cleveland Clinic score and the adapted St. Mark’s (Vaizey) score at 9 months compared with baseline.

#### Secondary end points included therapy acceptance and proportion of patients achieving continence or improvement in grade or frequency of incontinence.

***RESULTS:*** We enrolled 158 patients with anal incontinence. The median decrease in the Cleveland Clinic score from baseline to 9 months was 3 points greater for the triple target regimen than for EMG- biofeedback (95% CI, 1– 4; *P* = .0024). The improvement was 8 points for the triple target regimen (95% CI, 7–9) and 5 points for EMG-biofeedback (95% CI, 4 –7). Results were similar for the Vaizey score. Of patients treated for at least 3 months, continence was achieved by 50% of patients with the triple target regimen and 25.8% of those with EMG-biofeedback.

***CONCLUSIONS:*** The combination of amplitude- modulated medium-frequency electrostimulation with EMG-biofeedback in the triple target regimen is superior to EMG-biofeedback alone in the treatment of anal incontinence. Therapy programs for fecal incontinence are most effective if patients participate for longer than 2 to 3 months.

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Electrical stimulation and biofeedback for the treatment of fecal incontinence: a systematic review

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##### Abstract

*Purpose* This systematic review determines the best known form of biofeedback (BF) and/or electrical stimulation (ES) for the treatment of fecal incontinence in adults and rates the quality of evidence using the Grades of Recommendation, Assessment, Development, and Evaluation. Attention is giv- en to type, strength, and application mode of the current for ES and to safety.

*Methods* Methods followed the Cochrane Handbook. Ran- domized controlled trials were included. Studies were searched in The Cochrane Library, MEDLINE, and EMBASE (registration number (PROSPERO): CRD42011001334).

*Results* BF and/or ES were studied in 13 randomized parallel- group trials. In 12 trials, at least one therapy group received BF alone and/or in combination with ES, while ES alone was evaluated in seven trials. Three (four) trials were rated as of high (moderate) quality. Average current strength was report- ed in three of seven studies investigating ES; only two studies reached the therapeutic window. No trial showed superiority of control, or of BF alone or of ES alone when compared with

BF + ES. Superiority of BF + ES over any monotherapy was demonstrated in several trials. Amplitude-modulated medium- frequency (AM-MF) stimulation, also termed pre-modulated interferential stimulation, combined with BF was superior to both low-frequency ES and BF alone, and 50 % of the patients were continent after 6 months of treatment. Effects increased with treatment duration. Safety reporting was bad, and there are safety issues with some forms of low-frequency ES. *Conclusions* There is sufficient evidence for the efficacy of BF plus ES combined in treating fecal incontinence. AM-MF plus BF seems to be the most effective and safe treatment.

**Triple-Target Treatment Versus Low-Frequency Electrostimulation for Anal Incontinence**

##### A Randomized, Controlled Trial

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**SUMMARY**

Background: In the nonsurgical treatment of anal incontinence, the combination of amplitude-modulated medium-frequency stimulation and electromyographic biofeedback (EMG-BF), known as triple-target treatment (3T), is superior to EMG- BF alone. The aim of this trial is to compare 3T with the standard treatment, low- frequency stimulation (LFS).

Methods: 80 patients with anal incontinence of Grade I or higher who pre- sented to physicians or centers specialized in coloproctology were enrolled in this multicenter randomized trial with blinded observer. The trial had an open parallel-group design. Randomization was performed centrally by telephone. The primary endpoint was the Cleveland Clinic Score (CCS) after self-training at home with either 3T or LFS in two 20-minute sessions per day for 6 months.

The secondary endpoints included the proportion of patients regaining conti- nence, and the patients´ quality of life (QoL). On completion of the trial as planned, the results were evaluated with an intention-to-treat analysis. Study registration: DRKS00000138 (http://register.germanctr.de).

Results: 39 patients were randomized to 3T, and 41 to LFS. After 6 months of treatment, the CCS (mean ± standard deviation) was 3.1 ± 4.2 in the 3T group and 9.6 ± 3.9 in the LFS group. The median improvement in the CCS at 6 months compared to baseline was 7 points greater in the 3T group than in the LFS group (95% CI: 5–9, p<0.001). Anal continence was regained by 54% of the 3T patients, but none of the LFS patients (95% CI for the difference: 37.18% – 69.91%, p<0.001). QoL scores were higher in all dimensions in the 3T group than in the LFS group. No major adverse effects occurred in either group.

Conclusion: 3T is superior to LFS in the treatment of anal incontinence. The avail- able evidence suggests that the success of 3T is based on the combined effect of biofeedback and medium-frequency stimulation. LFS of the type applied in this trial has no effect. 3T should be used in routine clinical practice instead of LFS.

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# Benefit of anatomical-functional image fusion

**in the diagnostic work-up of neuroendocrine neoplasms**

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**Abstract.** The aim of this prospective study was to eval- uate anatomical-functional image fusion using the new technology of combined transmission and emission to- mography (SPET/CT) in patients with neuroendocrine tumours (NET). Fifty-four patients with known or sus- pected NET prospectively underwent both tumour scin- tigraphy with 111In-octreotide (*n*=43) or 123I-MIBG (*n*=11) and contrast-enhanced high-end spiral CT. Scin- tigraphy was performed using a gamma camera (Millen- nium VG & Hawkeye, GE) with an integrated X-ray tube for combined transmission and emission tomogra- phy. SPET and high-end CT were interpreted blinded with regard to localisation and classification of lesions. Analysis of fused images (SPET/CT) was done on a le- sion-by-lesion basis, followed by re-evaluation of SPET and high-end CT by consensus. The standard of refer- ence for confirming the presence or absence of malig- nancy was either histopathology or clinical and imaging follow-up data. A total of 120 lesions were identified by CT and/or scintigraphy. This group included four pa- tients with negative SPET but eight liver lesions on CT that were proven to be metastases. We excluded from the analysis two patients with no evidence of tumour on ei- ther modality, two lesions that lacked comparison with the standard of reference and two patients, each with two lesions, who were lost to follow-up. In 56 of the 114 evaluated lesions (49%), the results of SPET and CT were concordant; all lesions were interpreted as malig- nant. In 58 of 114 lesions (51%), consensus reading of fused images changed the image interpretation of 39 CT scans and 19 SPET studies: 31 lesions previously inter- preted as equivocal (*n*=10) or benign (*n*=21) were re-

#### classified as malignant and 27 lesions previously inter- preted as equivocal (*n*=19) or malignant (*n*=8) were re- evaluated as benign. The highest accuracy (99%) in clas- sifying NET lesions was achieved by combined analysis of SPET/CT (“hawkeye”) and high-end CT. The speci- ficity of SPET/CT was significantly higher than that of CT alone (*P*=0.0026) and slightly higher than that of SPET alone, but the accuracy of SPET/CT was inferior to that of side-by-side analysis of SPET and high-end CT (*P*=0.013) or visual correlation of SPET/CT and high- end CT (*P*<0.0001). Therapy was changed in 14 of 50 patients (28%) owing to the results of image fusion: in five patients tumour could be excluded, three patients were spared unnecessary surgery because of additional lesions indicating systemic tumour spread, in four pa- tients the surgical approach was changed owing to pre- cise tumour localisation and minimising of the surgical field, and in two patients medical and radiopeptide thera- py was changed. Anatomical-functional image fusion al- lows for improved localisation and characterisation of NET with resultant alteration of the treatment approach in a substantial proportion of patients.

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Treatment of chronic tinnitus with theta burst stimulation

A randomized controlled trial

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**ABSTRACT**

**Objective:** To test whether 4 weeks of bilateral repetitive transcranial magnetic stimulation (rTMS) to the temporal or temporoparietal cortex is effective and safe in the treatment of chronic tinnitus.

**Methods:** In this controlled 3-armed trial, 48 patients with chronic tinnitus were treated with 4 weeks (20 sessions) of bilateral continuous theta burst stimulation (cTBS) at the T¨ubingen Univer-

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sity Hospital. They were randomized to stimulation above the temporal cortex, the temporopari-

etal cortex, or as sham condition behind the mastoid. Patients were masked for the stimulation condition. Tinnitus severity was assessed after 2 and primarily 4 weeks of treatment and at 3 months follow-up with the tinnitus questionnaire and by a tinnitus change score. Audiologic safety was monitored by pure-tone and speech audiometry after 2 and 4 weeks of cTBS.

**Results:** Tinnitus severity was slightly reduced from baseline by a mean (SD) 2.6 (8.2) after sham,

2.4 (8.0) after temporoparietal, 2.2 (8.3) after temporal treatment of 16 patients each, but there was no significant difference between sham treatments and temporal (confidence interval [CI]

-5.4 to +6.7) or temporoparietal cTBS (CI -5.9 to +6.3) or real cTBS (CI -7 to +5.1). Patients’ global evaluation of tinnitus change after treatment did not indicate any effects. Audiologic mea- sures were unaffected by treatment.

**Conclusions:** Treating chronic tinnitus for 4 weeks by applying cTBS to the temporal or temporo- parietal cortex of both hemispheres appears to be safe but not more effective than sham stimula- tion. However, these results are not to be generalized to all forms of rTMS treatments for tinnitus.

**Classification of Evidence:** This study provides Class I evidence that bilateral cTBS is not effective in the treatment of chronic tinnitus. ***Neurology***® **2012;78:1–1**