Schwandner T, Hemmelmann C, Heimerl C, Kierer W, Kolbert G, Vonthein R, Weinel R, Hirschburger M, Ziegler A, Padberg W. Triple-Target Treatment Versus Low-Frequency Electrostimulation for Anal Incontinence A Randomized, Controlled Trial. DtschAblInt.

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 EMGBF alone. The aim of this trial is to compare 3T with the standard treatment, lowfrequency stimulation (LFS).

80 patients with anal incontinence of Grade I or higher who presented 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 continence, 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).

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.

3T is superior to LFS in the treatment of anal incontinence. The available 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.

Vonthein R, Heimerl T, Schwandner T, Ziegler A. Electrical stimulation and biofeedback for the treatment of fecal incontinence: a systematic review. Int J Colorectal Dis 2013; DOI 10.1007/s00384-013-1739-0

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 given to type, strength, and application mode of the current for ES and to safety.

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

BF and/or ES were studied in 13 randomized parallelgroup 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 reported 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 mediumfrequency (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.

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.

Schwandner T, König IR, Heimerl T, Kierer W, Roblick M, Bouchard R, Unglaube T, Holch P, Ziegler A, Kolbert G. Dis Colon Rectum. 2010 Jul;53(7):1007-16.

Triple target treatment (3T) is more effective than biofeedback alone for anal incontinence: the 3T-AI study.

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.

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.

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.

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.

Pfannenberg AC, Eschmann SM, Horger M, Lamberts R, Vonthein R, Claussen CD, Bares R.

Benefit of anatomical-functional image fusion in the diagnostic work-up of neuroendocrine neoplasms. Eur J Nucl Med Mol Imaging. 2003 Jun;30(6):835-43. Epub 2003 Apr 8.

The aim of this prospective study was to evaluate anatomical-functional image fusion using the new technology of combined transmission and emission tomography (SPET/CT) in patients with neuroendocrine tumours (NET).

Fifty-four patients with known or suspected NET prospectively underwent both tumour scintigraphy with (111)In-octreotide (n=43) or (123)I-MIBG (n=11) and contrast-enhanced high-end spiral CT. Scintigraphy was performed using a gamma camera (Millennium VG & Hawkeye, GE) with an integrated X-ray tube for combined transmission and emission tomography. 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 lesion-by-lesion basis, followed by re-evaluation of SPET and high-end CT by consensus. The standard of reference for confirming the presence or absence of malignancy 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 patients 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 either 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 malignant. 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 interpreted as equivocal (n=10) or benign (n=21) were re-classified as malignant and 27 lesions previously interpreted as equivocal (n=19) or malignant (n=8) were re-evaluated as benign. The highest accuracy (99%) in classifying NET lesions was achieved by combined analysis of SPET/CT ("hawkeye") and high-end CT. The specificity 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 patients the surgical approach was changed owing to precise tumour localisation and minimising of the surgical field, and in two patients medical and radiopeptide therapy was changed.

Anatomical-functional image fusion allows for improved localisation and characterisation of NET with resultant alteration of the treatment approach in a substantial proportion of patients.

Treatment of chronic tinnitus with theta burst stimulation: A randomized controlled trial

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To test whether 4 weeks of bilateral rTMS to the temporal or temporoparietal cortex is effective and safe in the treatment of chronic tinnitus.

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In this controlled three-armed trial, 48 patients with chronic tinnitus were treated with four weeks (20 sessions) of bilateral continuous theta burst stimulation (cTBS) at the Tübingen University Hospital. They were randomized to stimulation above the temporal cortex, the temporoparietal 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. Audiological safety was monitored by pure-tone and speech audiometry after 2 and 4 weeks of cTBS

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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 (CI -5.4 to +6.7) or temporoparietal cTBS (CI -5.9 to +6.3), nor between real cTBS (CI -7 to +5.1). Patients’ global evaluation of tinnitus change after treatment did not indicate any effects. Audiological measures were unaffected by treatment.

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Treating chronic tinnitus for 4 weeks by applying cTBS to the temporal or temporoparietal cortex of both hemispheres appears to be safe but not more effective than sham stimulation. However, these results are not to be generalized to all forms of rTMS treatments for tinnitus. This study provides class I evidence that bilateral cTBS is not effective in the treatment of chronic tinnitus.