NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Centre for Health Technology Evaluation

MTG Review Decision Document

Review of MTG5: The MIST Therapy system for the promotion of wound healing

This guidance was issued in July 2011.

NICE proposes an update of published guidance if the evidence base or clinical environment has changed to an extent that is likely to have a material effect on the recommendations in the existing guidance. Other factors such as the introduction of new technologies relevant to the guidance topic, or newer versions of technologies included in the guidance, will be considered relevant in the review process, but will not in individual cases always be sufficient cause to update existing guidance.

1. Recommendations

The guidance should be placed on the static list.

2. Original objective of guidance

To assess the case for adoption of The MIST Therapy system for the promotion of wound healing.

3. Current guidance

1.1 The MIST Therapy system shows potential to enhance the healing of chronic, 'hard-to-heal', complex wounds, compared with standard methods of wound management. If this potential is substantiated then MIST could offer advantages to both patients and the NHS.

1.2 The amount and quality of published evidence on the relative effectiveness of the MIST Therapy system is not sufficient, at the time of writing, to support the case for routine adoption of the MIST Therapy system in the NHS.

1.3 Comparative research is recommended in the UK to reduce uncertainty about the outcomes of patients with chronic, 'hard-to-heal', complex wounds treated by the MIST Therapy system compared with those treated

by standard methods of wound care. This research should define the types and chronicity of wounds being treated and the details of other treatments being used. It should report healing rates, durations of treatment (including debridement) needed to achieve healing, and quality of life measures (including quality of life if wounds heal only partially). It is recommended that centres using the MIST Therapy system take part in research that delivers these outcomes. Current users of the MIST Therapy system who are unable to join research studies should use NICE's audit criteria to collect further information on healing rates, duration of treatment and quality of life and publish their results.

1.4 NICE will review this guidance when new and substantive evidence becomes available.

4. Rationale

New relevant evidence has been published but it is inconclusive and does not fully address the claimed benefits in the scope. It is therefore proposed to transfer the guidance to the static list (see appendix 1 for explanation of options).

5. Implications for other guidance producing programmes

No comments were received from the other NICE guidance producing programmes

6. New evidence

The search strategy from the original assessment report was re-run on Medline, Embase, CDSR, Database of Abstracts of Reviews of Effects, PubMed, HTA database, CENTRAL, NHS EED, Econlit. References from December 2010 onwards were reviewed. Additional searches of clinical trials registries were also carried out and relevant guidance from NICE and other professional bodies was reviewed to determine whether there have been any changes to the care pathways. The company was asked to submit all new literature references relevant to their technology along with updated costs and details of any changes to the technology itself or the CE marked indication for use for their technology. The results of the literature search are discussed in the 'Summary of evidence and implications for review' section below. See Appendix 2 for further details of ongoing and unpublished studies**.**

The initial preparation of the review proposal by the MTEP team identified the need for a more detailed investigation which was carried out by the External Assessment

Centre, as described in section 8.2.1 of the published process and methods for reviewing medical technologies guidance.

6.1 Technology availability and changes

The MIST Therapy system has been subject to minor technical and manufacturing changes and is now marketed as the UltraMIST Therapy system, which is CE marked. The updated device has the same basic components, mode of action, indications and cost as the MIST Therapy system evaluated in MTG5.

6.2 Clinical practice

No specific references are given to NICE guidance or NICE pathways in the current management section of MTG5. Two relevant guidelines were identified, both of which postdate MTG5:

NICE guideline [NG19] Diabetic foot problems: prevention and management was updated in August 2015. This recommends one or more of the following as standard care for treating diabetic foot ulcers: offloading; control of foot infection; control of ischaemia; wound debridement; and wound dressings. Negative pressure wound therapy should be considered after surgical debridement for diabetic foot ulcers, on the advice of the multidisciplinary foot care service. Dermal or skin substitutes as an adjunct to standard care can be considered when treating diabetic foot ulcers, only when healing has not progressed, and on the advice of the multidisciplinary foot care service.

NICE guideline [CG179] Pressure ulcers: prevention and management was updated in April 2014. This recommends an assessment of the need for debridement which takes into consideration the amount of necrotic tissue; grade, size and extent of the pressure ulcer; patient tolerance and any co-morbidities. Where a need for debridement is identified, autolytic debridement, using an appropriate dressing should be used. Where this is likely to take longer and prolong healing time, sharp debridement should be considered. Following a skin assessment, systemic antibiotics should be offered to adults with a pressure ulcer if there are any of the following: clinical evidence of systemic sepsis; spreading cellulitis; underlying osteomyelitis. CG179 recommends that the type of dressing used should be made in consultation with the patient or carers, taking into account: pain and tolerance, position of the ulcer, amount of exudate, and frequency of dressing change. When treating grade 2, 3 and 4 pressure ulcers a dressing that promotes a warm, moist wound healing environment should be considered. Gauze dressing should not be used.

NICE medical technology guidance [MTG17] The Debrisoft monofilament debridement pad for use in acute or chronic wounds (2014) recommends the use of

the Debrisoft monofilament debridement pad as part of the management of acute or chronic wounds in the community.

The updates to the relevant guidelines do not impact the recommendations in MTG5, or the position of the technology in the current pathway. The technology is an adjunct to standard practice.

6.3 NICE facilitated research

The MTEP research facilitation workstream generated 2 pieces of new evidence in direct response to the Committee's research recommendations. The randomised controlled trial by White et al. (2015) and the technical study by Keltie et al (2013) are summarised in section 6.4.

6.4 New studies

Three systematic reviews, 6 randomised controlled trials, 2 cohort studies, 1 case report, 1 technical study and 1 cost-effectiveness analysis were identified in literature searches for relevant evidence published since the production of the guidance.

The Smith (2014) systematic review included 10 studies, 8 of which were assessed during development of MTG5. The remaining 2 studies used another device using ultrasound to deliver a saline mist to wounds, and are of limited generalisability to MTG5.

The Driver (2011) systematic review included 8 studies, all of which were already assessed during the development of MTG5.

The Voigt (2011) systematic review included 8 studies, 3 of which used MIST therapy on healing of chronic wounds and the remaining 5 studies used other different types of low-frequency ultrasound. No separate analyses were conducted on the results of the 3 MIST studies, of which 2 (Ennis et al. 2005; Kavros et al. 2007), were included in the guidance while the other appeared to be a conference abstract (Park et al. 2011) of the full paper by Yao et al. (2014). This conference abstract by Park et al. is no longer available online.

The study by Gibbons et al. (2015) was a multicentre RCT comparing MIST plus standard care (n=41) with standard care alone (n=40) in adult patients with venous leg ulcers. Total follow-up period was 11 weeks. The primary outcome was mean percent ulcer area reduction from randomisation to week 4, which was statistically significantly higher in the MIST compared with the standard care alone group (61.6% vs 45%, p= 0.02). Reductions were also statistically significant greater in the MIST group compared with the control in median (65.7% versus 44.4%) and absolute wound area (9.0 cm^2 versus 4.1 cm^2, p=0.003) as well as pain scores (from 3.0 to 0.6 versus 3.0 to 2.4, p=0.03).

The study by Prather et al. (2015) was a multicentre RCT comparing MIST plus standard care (n=16) with standard care alone (n=15) in patients with split thickness skin-graft donor sites. Follow up period was 5 weeks. The primary outcome measure was mean time to heal, which was significantly shorter in the MIST group than in the standard care alone (12.1 vs 21.3 days, p=0.04). All MIST subjects had epithelialised by 4 weeks, compared with 71% in the standard care group. Recidivism rate within the 6-week follow-up was 8% in the MIST compared with 45% in the standard care group, but the difference did not reach statistical significance. There was no significant difference between the two treatment groups in pain score reduction.

White et al. (2015) conducted a single centre RCT which compared MIST plus standard care (n=17) with standard care alone (n=19) in patients with chronic venous leg ulcers. Follow-up period was 13 weeks and then for those healed only there was a telephone follow-up 90 days later. The study found no statistically significant difference in the change from baseline to week 13 (or the point of healing) between the comparison groups, either in wound area, in health related quality of life score, or in reduction in pain score.

The Beheshti et al. (2014) study is a single centre RCT comparing the MIST therapy (n=30), high-frequency ultrasound therapy (HFU) (n=30) and standard treatment (n=30) for the healing of venous leg ulcers. Follow-up period was 6 months. The mean time of complete wound healing was statistically significantly shorter in both ultrasound therapy groups compared with the standard treatment (6.10 months MIST, 5.70 months, HFU 8.13 months, p<0.0001), and no statistically significant difference between the MIST and the HFU group (p=0.22). There was a statistically significant decrease in the size of ulcer, mean degree of pain and oedema in both ultra sound therapy groups after the 4-month visit in comparison to the standard treatment group; the difference was not significant between the MIST and HFU groups. No significant differences between groups in the recurrence of venous leg ulcers during a 6-month follow up after complete wound healing were observed.

The Yao et al. (2013) study was a single centre pilot RCT with 3 comparison groups in 12 patients with 12 non healing diabetic foot ulcers: MIST thrice per week (n=4), MIST once per week (n=4), and no MIST (n=4). Follow-up period was 5 weeks. The group receiving MIST thrice per week showed statistically significant wound area reduction at weeks 3, 4 and 5 compared to baseline, with the greatest percent area reduction (86%). The presence of wound area reduction in the group receiving MIST twice per week and that without MIST was 25% and 39%, respectively, but there were no statistically significant differences between these two groups over time.

The Olyaie et al. (2013) study was a single centre RCT comparing 3 treatment methods in outpatients with venous leg ulcers: MIST therapy (n=30), HFU therapy (n=30), and standard care (n=30). Total follow-up period was not clear but appeared to be at least 12 months. No significant differences at 2 months between the 3 groups in mean ulcer size, oedema, and pain score were observed. At 4 months

significant differences were observed between the 3 groups in ulcer size, number of patients with decreases in oedema, and pain scores, with the MIST group having the best results, followed by the HFU group and then the standard care group. There were also statistically significant differences in time to complete wound healing, with the MIST group having the shortest time duration, followed by HFU and then standard care.

The Honaker et al. (2013) was a retrospective cohort study in 85 patients with 127 suspected deep tissue injuries. MIST plus standard care (43 subjects with 64 wounds) was compared with standard care (42 subjects with 63 wounds). Follow-up period was not clear. The MIST group had a statistically significant improvement in overall wound severity compared with the standard care group. A greater proportion of MIST patients were discharged home (21%) compared with the control arm (12%) and fewer were discharged to a long-term care facility (10% from the MIST group compared with 33% from the standard care group).

The study by Escandon et al. (2012) was a small prospective single arm cohort study of MIST treatment for patients with refractory venous leg ulcers (n=10). Follow-up period was 4 weeks. Following 4 weeks of MIST treatment, there was a statistically significant reduction in wound area, but no statistically significant reduction in individual and total bacterial counts, inflammatory cytokine expression, and pain score.

Norris and Henchy (2010) reported 4 cases who received MIST treatment for non-healing leg ulcers in a UK leg ulcer clinic. The wound reduction rates were between 41–73% over a 10–14 week treatment period. Clinicians found the MIST Therapy system easy to use with minimal training. It was non-invasive, pain-free and did not result in discomfort or side-effects for the patients.

Amir (2014) reported a cost-effectiveness analysis of the MIST plus standard care compared with standard care alone for non-healing diabetic foot ulcers from a US healthcare system perspective. The key clinical parameter was healing rate for which data were taken from different trials. Cost data were derived from a study using claims data in the US during 2000 and 2001. The estimated cost saving over 12 weeks was $2,016.324 per 1,000 patients. The saving was due to reduced time to heal, reduction in the costs of subsequent medical care and reduction in the chance of costly complications.

Keltie et al. (2013) was a laboratory study to determine the frequency and intensity of ultrasound transmission with and without the saline mist, using phantom tissues. It found that transmission of the ultrasound wave was not attenuated by the saline mist, and that in the absence of the saline mist, only 0.1% of the ultrasound intensity would be delivered into the wound site.

7. Summary of new evidence and implications for review

The EAC concluded that the additional studies on the effectiveness of MIST identified since the development of MTG5 provide some limited extra comparative data with longer follow-up. However, it judged that although this may in part reduce the degree of uncertainty on the effectiveness of MIST it does not fully address the scope of the original evaluation. In summary, the new evidence is unlikely to have a material effect on the recommendations in the published guidance.

8. Implementation

No relevant information was available.

9. Equality issues

No equality issues were identified in the original guidance

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Appendix 1 – explanation of options

If the published Medical Technologies Guidance needs updating NICE must select one of the options in the table below:

Options	**Consequence**	**Selected – 'Yes/No'**
Standard update of the guidance	A standard update of the Medical Technologies Guidance will be planned into NICE's work programme.	No
Update of the guidance within another piece of NICE guidance	The guidance is updated according to the processes and timetable of that programme.	No

If the published Medical Technologies Guidance does not need updating NICE must select one of the options in the table below:

Options	**Consequences**	**Selected – 'Yes/No'**
Transfer the guidance to the 'static guidance list'	The guidance remains valid and is designated as static guidance. Literature searches are carried out every 5 years to check whether any of the Medical Technologies Guidance on the static list should be flagged for review.	Yes
Defer the decision to review the guidance to	NICE will reconsider whether a review is necessary at the specified date.	No
Withdraw the guidance	The Medical Technologies Guidance is no longer valid and is withdrawn.	No

Appendix 2 – supporting information

Relevant Institute work

Published

NICE guideline (2015) Diabetic foot problems: prevention and management [NG19]

NICE guideline (2014) Pressure ulcers: prevention and management [CG179]

Registered and unpublished trials

Trial name and registration number	Details
Trial NCT02045303: Healing Rate of Leg Wounds Treated With Contact and Noncontact Ultrasound: The VIP Ultrasound Protocol	Interventional – Efficacy study Estimated study completion date: December 2015

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