EXTERNAL ASSESSMENT CENTRE REPORT

Title: moorLDI2-BI a laser Doppler blood flow imager for burn wound assessment. V2

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Declared interests of the authors

None

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Rider on responsibility for report

The views expressed in this report are those of the authors and not necessarily those of NICE. Any errors are the responsibility of the authors.

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Abbreviations

ANZBA	Australian and New Zealand Burns Association
CE	Conformité Européenne (European Conformity)
CRD	Centre for reviews and dissemination
EAC	External assessment centre
EED	Economic evaluation database
FDA	Food and drugs administration
HRG	Health resource groups
LDI	Laser Doppler imager/imaging
MeSH	Medical subject heading
MHRA	Medicines and Healthcare products Regulatory Agency
NHS	National Health Service
NICE	National Institute for Health and Clinical Excellence
RCT	Randomised controlled trail
TBSA	Total body surface area

Note on use of page numbers

Page numbers shown in parentheses in this External Assessment Centre (EAC) report refer to the manufacturer submission document, unless otherwise stated. References to the assessment report are given in terms of section number (e.g. ‘see Section 4.1.4 for details’).

Note on appendices

Appendices A, B, etc and 1, 2, etc refer to the manufacturer submission. Appendices One, Two, etc refer the EAC report.

1. Summary

1.1 Scope of the submission

This report assesses the submission to NICE by the manufacturer (Moor Instruments Ltd) covering the use of moorLDI2-BI burn wound assessment imager. Specifically, the submission considers the moorLDI2 burn imager for the assessment of patients with intermediate level burns, which is in line with the scope issued by NICE for the appraisal. This report includes an assessment of both clinical effectiveness and the cost implications, based on evidence submitted by the manufacturer.

1.2 Summary of submitted clinical effectiveness evidence

Eleven studies are included in the evidence for clinical effectiveness relating to patients with intermediate level burn wounds in which the moorLDI2 was used for the assessment of the burns. Most of the studies were observational and two were audits. One study was an in depth statistical analysis. All studies were done at burn centres in the UK and worldwide and covered a 14 year period. One study included an MHRA registered multi-centre clinical investigation. None of the studies was funded by Moor Instruments Ltd or by any other manufacturer except for the MHRA approved study. This study was supported by the manufacturer who was in turn supported by a SMART DTI grant. A statement regarding conflict of interest published by the clinical project partners is as follows:

The LDI equipment used during this investigation was loaned by Moor Instruments Ltd. to four of the burn centres and subsequently gifted to these institutions. At the fifth burn centre the equipment was purchased already and Moor Instruments Ltd. subsequently made an equivalent donation for unrestricted research. Moor Instruments Ltd. funded travel and accommodation for meetings during the design of the investigation and provided technical support at all stages of the investigation.

The studies compared the use of the moorLDI2 to clinical assessment and/or biopsy for the assessment of burn wounds and the accuracy in prediction of

healing time. The studies demonstrated that the use of moorLDI2 in combination with clinical assessment enables more accurate prediction of healing time compared to clinical assessment alone and can result in earlier surgical decisions.

1.3 Summary of submitted economic evidence

The literature searches conducted by the manufacturer do not identify any relevant economic studies. However, a number of studies were used to provide the data for the cost model, such as Hemington-Gorse *et al* (2009), Griffiths *et al.*

The model estimates the cost savings to the NHS by the introduction of the moorLDI2 for the assessment of burns of an indeterminate depth. The savings, generated by reduced length of hospital stay and fewer or shorter operations were calculated per patient by a bottom-up costing approach. A period of seven to eight days of hospitalisation has been taken as the time horizon of the model.

For patients with intermediate burns, the manufacturer reports that, if a range of 10% to 100% of those admitted are scanned the NHS will save from £1055 to £4594 per patient scanned. The break even points for the base case for the NHS as a whole (28 centres) is 576 patients admitted or 403 patients scanned for the leasing option and 485 patients admitted or 340 scanned for the purchasing option. The deterministic sensitivity analysis identified the key driver of the analysis to be the number of patients scanned.

1.4 Commentary on the robustness of submitted evidence

1.4.1 Strengths

The clinical effectiveness evidence is based on studies undertaken at burn centres in the UK and worldwide. The studies performed with the moorLDI2 covered a period of 14 years and included an MHRA registered multi-centre clinical investigation. The accuracy in the prediction of healing time and the decision for surgery in burn wounds reported in the analysis of the studies are considered clinically important.

In general the cost analysis is adequate in addressing the decision problem. The analysis estimated cost savings from the use of the moorLDI2 in classifying intermediate burn wounds in the NHS with a sensible choice of model parameters for realistic clinical scenarios.

1.4.2 Weaknesses

The clinical effectiveness evidence is based on non-randomised data, observational studies and audits. Studies of such design can potentially introduce bias.

The search strategy used in the identification of the studies is considered appropriate by the EAC. However it is inadequately reported in the submission Therefore the EAC cannot be confident that all the relevant studies have been identified.

In a supplementary document (Excel spreadsheet) provided by the manufacturer it is noted that the results of an additional study (Nguyen *et al.*) are provided. This study was not included in the final eleven studies identified by the manufacturer (it was however included in Appendix A: bibliography, References (page 97)).

The literature search for cost analysis is considered appropriate but not adequately reported in the manufacturer's submission document. The search did not identify any relevant studies; however a number of studies are used to provide the data for the cost analysis model. The heavy reliance on data from Hemington-Gorse *et al* may be considered a weakness, but given the lack of economic studies identified in the literature search this is acceptable.

1.4.3 Areas of uncertainty

The EAC is not confident about the identification of studies from the literature searches that were conducted both for clinical effectiveness and cost analysis.

1.5 Key issues

No key issues were identified.

2 Background

2.1 Critique of manufacturer's description of underlying health problem

The submission provides details of the effectiveness and accuracy of the laser Doppler imager as a non-invasive tool for the assessment of burn depth. It focuses on patients admitted to hospital with burn wounds of mixed depth that require assessment of their wounds to support the choice of wound dressings and to decide which burn areas require grafting.

Relevant information is provided in relation to the expected healing potential and improvement of treatment decisions and the number of patients assumed to be eligible for treatment in England and Wales, based on findings from the National Burn Care Review Committee Standards and Strategy for Burn Care.

2.2 Critique of overview of current service provision

The scope defined by NICE, describes several options for assessment of burn wounds.

Clinical assessment, one of the current practices included in the scope, is described in the manufacturer submission as being the most widely used method of assessing burn wound depth. Evidence about the use of comparators and the intervention is not featured in the current service provision overview; however this is covered in later sections.

The submission points out that the accurate assessment of burn depth is important in making the decision about treatment of the burn and laser Doppler imaging is primarily relevant to the improvement of treatment decisions. The submission states that the decisions to graft for intermediate thickness burn wounds based on a clinical assessment alone 'are wrong in a significant number of cases'. A best practice for a clinical assessment protocol is not described and the accuracy depends largely on individual clinician's experience. The submission includes evidence to support the latter claim (page 11).

The submission refers to the potential adverse events that include damage to the retina of the patients not wearing the recommended eye protection and staring into the laser beam and points out that no such events have been reported.

The manufacturer states that the main resource implication to the NHS associated with the use of moorLDI2 is the system operation. This is in terms of staff training to operate the system effectively and safely and to correctly interpreting the image in relation to diagnosis. The costs of training the staff are included in the sale/lease price.

Other costs include the electricity required to power the system and the colour ink printer. Administrative and IT costs should also be included if the moorLDI2 is networked with a specialist digital imaging database such as DICOM.

No other significant costs are reported.

3 Critique of definition of decision problem

3.1 Patient population

Patients with intermediate burns are considered as being relevant in the scope issued by NICE. The submission focuses on this population.

3.2 Intervention

The intervention considered in the submission is the moorLDI2 burn wound assessment imager. The intervention is based on the relationship between burn depth and subsequent changes in the microvascular blood flow in the dermis. The technology provides an estimate of perfusion through the burn wound, based on the principal that a lower perfusion correlates with a deeper wound, and therefore a longer time to heal. The submission states that 'a low power Helium-Neon red laser beam is directed at the burn wound via a mirror. It is scanned in raster fashion across the burn area by rotating the mirror about vertical and horizontal axes. There is no direct contact with the tissue being assessed. Penetration depth is the full dermis. Laser light scattered from moving blood cells in the tissue undergoes a Doppler frequency shift, the average frequency shift being proportional to the average speed of the blood cells. Some of the scattered laser light is collected by the mirror and then focussed, by light-collecting lenses, on photodiode detectors. The resulting photocurrent is processed to calculate the blood flow in the tissue and this information is displayed as a colour-coded map of the wound area'.

The manufacturer submission states that the moorLDI2-BI has been CE marked as a burn wound assessment imager.

3.3 Comparator

The possible comparators for moorLDI2 are identified in the NICE scope as clinical assessment of burns, biopsy, ultrasound, injection of vital dyes to stain living tissue, fluoroscein injection and thermography. However, the submission identifies the clinical assessment as the only comparator routinely used in clinical practice for assessing the depth of burn wounds.

No comparator was used in the cost effectiveness modeling.

3.4 Outcomes

The outcomes included in the manufacturer submission are consistent with the NICE scope. The clinical outcomes considered in the submission are accuracy to predict healing potential treatment decision and time to surgery, and length of hospital stay. Other important outcomes are the sensitivity, specificity and positive and negative predictive values of the wound healing potential within 14 to 21 days. Although additional outcomes are featured in the scope, the submission includes the outcomes that are considered clinically significant by the included studies. No safety outcomes or adverse events are reported.

3.5 Time frame

The analysis provided in the analysis of cost section in the manufacturer submission is based on the period of hospitalisation (seven to eight days), as the main benefits of laser Doppler imaging in terms of resource savings are expected to be during this period. Therefore, the submission states that extrapolation of results beyond this period was not considered necessary.

3.6 Other relevant factors

The manufacturer submission acknowledges that the interpretation of images requires consideration of a number of potential confounding factors such as patient movement during scan, wound infection, undebrided wounds imaged etc. The manufacturer states that all these factors are described in the Users' Guide.

3.7 Equality and diversity issues

No equality and diversity issues are identified to be addressed in the submission for the use of moorLDI2. The moorLDI2 is suitable for use of all patients irrespective of age, gender or ethnicity.

4 Clinical effectiveness

4.1 Critique of manufacturer's approach

4.1.1 Description and critique of the manufacturer's identification and selection of studies.

Assessment of literature searches

The moorLDI2 burn imager is a non-invasive, non-contact burn wound assessment device and the submission presents evidence about the product and its effectiveness in the assessment of burn depth which is used in the prediction of healing time and/or the need for skin grafting.

The search strategy used in the identification of the studies is considered appropriate. However it is inadequately presented in the submission. There is a lack of detail in the description of the manufacturers' searches for studies. The following critique is based on the information provided in the submission in Appendix 2: Search strategy for section 5.1 (Identification of studies), page 99.

The submission includes searches in the PubMed, Cochrane Library, ScienceDirect, Biomedical Central, Medline and Burns Journal, but it does not include a search in Embase. The search strategy is presented in Appendix 2 section 7.2.4 (page 100) which the EAC assumed was followed in all the searched databases.

The terms used in the search strategy presented in the submission are considered to be appropriate. However, the EAC noted the absence of the use of any subject index headings (for example, MeSH), which has the risk of missing relevant studies.

The submission states that the date span of literature searches was limited to 1990 to the present for burn assessment specifically using the Moor Instruments Ltd laser Doppler imaging system, which is also considered by the EAC to be the correct strategy.

There is no indication that any other limits are applied to the search strategy.

The submission also states that additional searches were performed regarding competitors' websites and literature searches for competitors' equipment to identify any comparative studies. Searches to identify material published or presented at conferences are also reported to be performed by the manufacturer on a regular basis. These searches include specific society websites including the British Burn Association, Australia New Zealand Burn Association and associated publications including abstract/meeting proceedings. However, there is no indication in the submission of any specific studies identified by these searches.

The searches for evidence on adverse events are reported in Appendix 4: search strategy for section 5.9 (Adverse events), page113. The submission includes a search in PubMed (which includes Medline and Medline In-process) and ScienceDirect but does not include a search in Embase and Cochrane Library.

The search strategy for evidence on adverse events even though appropriate, is inadequately reported in the submission. It is lacking in detail, does not include indexing terms or synonyms and it is not clear whether any limits were applied. The submission includes one search strategy but it is not specified in which database it was applied. The EAC assumed it was followed in all the searched databases.

Use of inclusion/exclusion criteria in the selection of studies

The submission includes two tables for the inclusion/exclusion criteria in the selection of studies, one in section 5.2.1 and a slightly more detailed one in Appendix 2, section 7.2.6 (page 102). It was assumed that the criteria presented in the second table were the correct ones.

The inclusion criteria used for the selection of studies in the manufacturer submission are consistent with the decision problem and therefore are considered to be appropriate. Patients included are those with burn injuries, both adult and paediatric, male and female. The intervention eligible for

inclusion is laser Doppler imager of burn wounds with CE marked, 510K FDA approved equipment. The included outcomes are time to healing, scarring, length of hospital stay, cost reduction, time to surgery and treatment decision and burn depth by biopsy. The remaining outcomes specified in the scope (number of operations and their duration, number of dressing changes and wound complications) are not featured in the inclusion criteria. The search strategy is restricted to English language records. Study design (audits, clinical studies, pilot studies, observational studies, cohort studies and statistical studies) were included. Only fully published articles and papers submitted for publication (in press) are included.

The exclusion criteria excluded studies where laser Doppler imaging was not used or when a laser Doppler device without CE marking or 510K FDA approval was used. Studies in any language other than English were also excluded as well as unpublished audits and posters.

The submission includes some information on the data abstraction strategy such as the number of reviewers who screened the studies and applied the inclusion/exclusion criteria. However, it is not clear from the search strategy how the number of studies identified in the search (number of hits) was limited to 21.

In total from the 21 studies identified, 11 are included in the review, with the remaining 10 studies excluded as they were published as abstracts of oral presentations or abstracts of poster presentations at national and international burns meetings. The included studies which make up the clinical effectiveness evidence are:

1. Hoeksema *et al.* 2009 (Accuracy of early burn depth assessment by laser Doppler imaging on different days post burn)

2. Mill *et al.* 2009 (Laser Doppler imaging in a paediatric burns population)

3. Brown *et al*. 1998 (The use of laser Doppler imaging as an aid in clinical management decision making in the treatment of vesicant burns)

4. Kim *et al*. 2010 (The Impact of Laser Doppler Imaging on Time to Grafting Decisions in Paediatric Burns)

5. Pape *et al.* 2001 (An audit of the use of laser Doppler imaging (LDI) in the assessment of burns of intermediate depth)

6. Holland *et al*. 2002 (Laser Doppler imaging prediction of burn wound outcome in children)

7. Niazi *et al.* 1993 (New laser Doppler scanner, a valuable adjunct in burn depth assessment)

8. La Hei *et al.* 2006 (Laser Doppler Imaging of paediatric burns: Burn wound outcome can be predicted independent of clinical examination)

9. Monstrey *et al.* in press (Burn wound healing time assessed by laser Doppler imaging, Part 2: validation of a dedicated colour code for image interpretation)

10. Baker *et al.* 2009 (Using ordinal logistic regression to evaluate the performance of laser-Doppler predictions of burn-healing time)

11. Jeng *et al.* 2003 (Laser Doppler Imaging determines need for excision and grafting in advance of clinical judgement: a prospective blinded trial)

4.1.2 Identified studies - studies included in and excluded from the submission

Eleven clinical effectiveness studies are identified as being relevant by the manufacturer in their submission. Ten of these studies have been published and one (9) has been submitted for publication (in press). Two are non-randomised studies (1, 4), five are observational studies (2, 3, 6, 7, 9), one is a blinded trial (11) and two are audits (5, 8). One study (10) is an in-depth statistical analysis of data from the Monstrey *et al.* study. One study includes only adult patients (7), four studies include only paediatric patients (2, 4, 6, 8), and four include both adult and paediatric patients. One study (3) is an animal study. The studies are not gender specific with the exception of the animal

study where only female pigs were used. All studies include inpatients and outpatients presenting with intermediate depth burn wounds.

The included animal study involved white female pigs and investigated the possible use of LDI as an aid in clinical decision making in the treatment of vesicant burns.

None of the studies were funded by Moor Instruments Ltd or any other manufacturer except for the MHRA approved study. This study was supported by the manufacturer who was in turn supported by a SMART DTI grant. A statement regarding conflict of interest published by the clinical project partners is as follows:

The LDI equipment used during this investigation was loaned by Moor Instruments Ltd. to four of the burn centres and subsequently gifted to these institutions. At the fifth burn centre the equipment was purchased already and Moor Instruments Ltd. subsequently made an equivalent donation for unrestricted research. Moor Instruments Ltd. funded travel and accommodation for meetings during the design of the investigation and provided technical support at all stages of the investigation. They were all conducted in burn centres in UK and worldwide. The follow up time varied from 12 days to six weeks or until healing or grafting. The animal study had a seven day follow up.

Seven studies evaluated the use of LDI compared to clinical assessment and/or biopsy in terms of prediction of healing time. Three studies (2, 6, 9) investigated the accuracy of LDI in predicting healing time with no other comparator. One study (9) validated the use of the dedicated colour palette and described clinical and technical factors during interpretation of the LDI images.

Details of the studies that are excluded from the submission and the reasons behind the exclusions are provided in the submission document (pages 23 to 25). All excluded studies had not been peer reviewed or published. These studies are shown below:

- Barques *et al.* 2007 (poster only): evaluation of the accuracy and reliability of LDI compared to clinical assessment for burn depth diagnosis
- Barnwell *et al.* 1998 (abstract only): investigation of the predictive value of the LDI and its accuracy for assessment large burn areas.
- Holland *et al.* 2001 (abstract only): prediction of burn wound outcome in children
- Jeng *et al.* 2001 (abstract only): LDI as an aid to clinical judgement of intermediate depth burns
- La Hei *et al.* 2002 (abstract only): accuracy of LDI
- Monstrey *et al.* 2001 (presentation and abstract only): accuracy and cost effectiveness of LDI
- Monstrey *et al.* 2004 (presentation and abstract only): use of LDI to predict a better functional or aesthetic outcome by early surgery or conservative therapy
- Pape *et al.* 1998 (presentation and abstract only): LDI as a tool for the assessment for burn depth
- Spence *et al.* 2004 (presentation and abstract only): Scanning laser Doppler imaging for burn depth assessment

The manufacturer submission identifies several relevant ongoing studies. These include:

Presentations at the ANZBA meeting (Darwin, Australia 5-8 Oct 2010)

- Cuttle *et al.* (The effect of correct first aid treatment on the vasculature and cells within a burn)
- Jayalath *et al.* (Clinical relevance of laser Doppler Imaging in adult burns)
- Ward *et al.* (MoorLDIS-BI trial against MoorLDI2-BI for burn wound depth assessment)

- Wang *et al.* (Ultrasound assessed thickness of burn scars in association with Laser Doppler determined depth of burns in paediatric patients.)

Papers submitted for publication in the Burns Journal

- Pape *et al.* (Burn wound healing time assessed by laser Doppler imaging (LDI) Part1: derivation of a dedicated colour code for image interpretation)

- Monstrey *et al.* (Burn wound healing time assessed by laser Doppler imaging (LDI) Part2: Validation of a dedicated colour code for image interpretation)

The two papers submitted for publication in the Burns Journal were supplied by the manufacturer when requested by the EAC.

Include details of any relevant studies that were not included in the submission

The search strategy followed by the manufacturer in the submission was, in general, considered appropriate but not sufficiently detailed. When the EAC re-ran the search in PubMed (as close to that described in the manufacturer submission as possible), a number of relevant studies were identified that was not included in the manufacturer submission. The EAC assumed that the manufacturer was aware of these studies, as four of them were included in the bibliography and references in Appendix A (pages 93 to 97); however the reason for their exclusion is not stated in the submission.

A list of studies identified by the EAC search that are not included in the submission but are considered relevant by the EAC is shown in Appendix One. These studies were carried out in burn centres in the UK and worldwide, all were considered relevant to the decision problem.

Jaskille *et al* (2010) performed a critical assessment of the burn literature on the LDI and a review of the Doppler principle and how the LDI uses it to estimate perfusion. They concluded that although more uniform and systematic research is needed, LDI is a reliable aid to the clinical prediction of healing.

Nguyen *et al* (2009) investigated the ability of LDI to predict burn wound outcome in paediatric patients prior to and after 48 hours from the time of injury. They concluded that LDI performed prior to 48 hours after injury was as accurate as a scan completed after 48 hours in differentiating between deep and superficial wounds in the paediatric burns.

The impact of burn wound dressings on LDI assessment of a cutaneous injury model was investigated by Holland *et al* (2007) in a pilot study. They found that different types of dressing and different ways of applying them affected the output measurement.

Wang *et al* (2010) investigated the assessment of burn scars using ultrasound in association with laser Doppler imaging in order to determine depth of burns in paediatric patients. Their study indicated that LDI can be used for predicting the risk of hypertrophic scarring and for guiding burn care.

Hemington-Gorse (2005), Mandal (2006) and Sainsbury (2008) have critically evaluated the clinimetrics of LDI in burn assessment and its ability to differentiate between deep and superficial burns. All these reviews concluded that LDI when used together with clinical assessment can improve the quality of burn care.

The EAC found that none of the additional studies contradicted the outcomes of the studies included in the manufacturer submission and, in general, supported the use of LDI for the assessment of burn wounds.

4.1.3 Description and critique of manufacturers approach to validity assessment and details of the quality assessment of studies.

A critical appraisal of all identified studies was undertaken by the manufacturer. The manufacturer assessed the quality of the clinical effectiveness studies using appropriate criteria. The submission states that the checklist used was based on the criteria for assessment on risk of bias in RCTs, issued by the Centre for Reviews and Dissemination guidance for undertaking reviews in health care, but it had been modified by the manufacturer as the included in the submission studies did not include any

RCTs. These modifications are considered appropriate by the EAC. The checklist used captured the main characteristics of the quality of the studies.

The 11 studies included in the submission were assessed by a minimum of two reviewers. The manufacturer's comments regarding the studies' approach to addressing the areas covered by the questions can be seen in Table 1 alongside comments by the EAC. However, three studies have not been included in section 7.3 Appendix 3: Quality assessment (pages 103-111).

Table 1: Critical appraisal of clinical effectiveness studies

Hoeksema *et al.* (2009)		
What is the accuracy of early burn depth assessment by Laser Doppler Imaging on different days post burn?	**How is the question addressed in the study?**	**Comments by EAC**
Study type – cohort, observational, case studies.	Prospective evaluation and comparison study	Non-randomised cohort study
Is the sample size adequate for the study?	N=40, No power calculations or sample size analyses were provided in the methodology of this study	-
Selection criteria for subjects?	Insufficient detail is provided in the methodology with regards to patient selection	-
Appropriateness of study design to study question	The study has been designed to address the study question.	-
Were participants/care providers/outcome assessors blind to Laser Doppler Imaging images? If not, how could this affect the risk of bias?	All care givers, clinical assessors and observers were unaware of Laser Doppler Imaging results. Burn wounds were managed according to clinical assessment only.	Blinded study
Were there unexpected drop outs/exclusions during the study which were inadequately explained?	No patients withdrew or were excluded but in some cases patients were not scanned on all details. Reasons were provided.	-
Is the choice of outcome measures appropriate to the study question?	All outcome measures were specific to the study question.	-
Were appropriate statistical analyses presented?	Yes, statistical analysis has been provided.	A Mann-Whitney U-test was used to assess the statistical significance
Quality of intervention with Laser Doppler Imaging – is scan timing appropriate?	Yes, Laser Doppler Imaging was performed on 5 days.	-
Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination		

Mill *et al.* (2009)		
Can Laser Doppler Imaging be used to predict burn wound outcomes in a paediatric population?	**How is the question addressed in the study?**	**Comments by EAC**
Study type – cohort, observational, case studies.	Case series, subject to bias of an observational study.	Non comparative study
Is the sample size adequate for the study?	N=48, No details or power analyses provided on subject selection.	48 paediatric patients, 85 wounds
Selection criteria for subjects?	Insufficient details provided.	Children presented from 0 to 190 hours post injury.
Appropriateness of study design to study question	Study design was appropriate – based on paediatric population and appropriate measures of outcome.	-
Were participants/care providers/outcome assessors blind to Laser Doppler Imaging images? If not, how could this affect the risk of bias?	Surgeons not blind to Laser Doppler Imaging, authors state this may include bias	-
Were there unexpected drop outs/exclusions during the study which were inadequately explained?	It appears 4 patient's results have not been included and these are unexplained.	Patients that were in pain during wound dressing were not scanned
Is the choice of outcome measures appropriate to the study question?	Outcome measures entirely appropriate and relevant to study questions and results address initial aim.	-
Were appropriate statistical analyses presented?	All results documented clearly in tables and graphs, minitab statistics package used and significant logical regression statistics.	-
Quality of intervention with Laser Doppler Imaging – is scan timing appropriate?	Scanning time earlier than recommended by manufacturer but was entirely appropriate for the study question.	Manufacturer recommends 48 to 72 hours post injury
Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination		

Brown *et al.* (1998)		
Can Laser Doppler Imaging be used as an aid in clinical management decision making in the treatment of vesicant burns?	**How is the question addressed in the study?**	**Comments by EAC**
Study type – cohort, observational, case studies.	Pilot study – animals	-
Is the sample size adequate for the study?	N=8 Very small sample size but appropriate for a pilot study	-
Selection criteria for subjects?	Yes, for the purpose of this study	-
Appropriateness of study design to study question	No in the fact the study questions does not mention use of pigs as a subject but suggests 'human' involvement by mentioning clinical management: use of vesicant agents and skin burns.	-
Were participants/care providers/outcome assessors blind to Laser Doppler Imaging images? If not, how could this affect the risk of bias?	n/a	-
Were there unexpected drop outs/exclusions during the study which were inadequately explained?	No	No unexpected drop outs are reported
Is the choice of outcome measures appropriate to the study question?	Yes, biopsies were taken (gold standard)	-
Were appropriate statistical analyses presented?	n/a	-
Quality of intervention with Laser Doppler Imaging – is scan timing appropriate?	n/a	-
Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination		

Kim *et al.* (2010)		
Is there evidence that Laser Doppler Imaging in paediatric patients leads to earlier decision making of the need for operative intervention to ensure optimal burn wound healing?	**How is the question addressed in the study?**	**Comments by EAC**
Study type – cohort, observational, case studies.	Non-randomised cohort study	Data were reviewed retrospectively
Is the sample size adequate for the study?	Yes a large sample size was used (196)	One group (49%) had a LDI scan, the other was clinically assessed.
Selection criteria for subjects?	Yes, selection criteria and exclusion criteria provided in full detail and sufficient not to introduce bias due to patient selection	-
Appropriateness of study design to study question	Completely appropriate design of study to answer the study question	-
Were participants/care providers/outcome assessors blind to Laser Doppler Imaging images? If not, how could this affect the risk of bias?	No – treating surgeon viewed Laser Doppler Imaging in order to decide on need of operative intervention	-
Were there unexpected drop outs/exclusions during the study which were inadequately explained?	No unexplained exclusions/drop outs	-
Is the choice of outcome measures appropriate to the study question?	Yes all outcome measures are appropriate	-
Were appropriate statistical analyses presented?	Yes, appropriate statistical analyses presented including one-way ANOVA, student t-test. Pearsons X2 were applied to categorical data	The study incorporates a detailed statistical analysis
Quality of intervention with Laser Doppler Imaging – is scan timing appropriate?	Scan timing was described as recommended by the manufacturer	-
Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination		

Pape *et al.* (2001)		
How accurate is Laser Doppler Imaging assessment of intermediate depth burns compared to clinical assessment?	**How is the question addressed in the study?**	**Comments by EAC**
Study type – cohort, observational, case studies.	Prospective audit	-
Is the sample size adequate for the study?	N=48 for a 6 month audit the sample size appears adequate	48 patients with 76 burns
Selection criteria for subjects?	The author describes the audit of patients admitted with intermediate burns. Assuming these were all patients during the 6 month period. No bias was introduced	-
Appropriateness of study design to study question	Study design was very appropriate to the study question.	-
Were participants/care providers/outcome assessors blind to Laser Doppler Imaging images? If not, how could this affect the risk of bias?	Clinical assessment was performed and documented prior to Laser Doppler Imaging assessment.	No blinding
Were there unexpected drop outs/exclusions during the study which were inadequately explained?	No	No drop outs were reported
Is the choice of outcome measures appropriate to the study question?	Yes all appropriate	-
Were appropriate statistical analyses presented?	No statistical analyses was presented	-
Quality of intervention with Laser Doppler Imaging – is scan timing appropriate?	Yes all scans performed 48-72 hours post burn within manufacturers guidelines	-
Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination		

Holland *et al.* (2002)		
What is the ability of Laser Doppler Imaging in evaluating burn depth in children	**How is the question addressed in the study?**	**Comments by EAC**
Study type – cohort, observational, case studies.	Observational pilot study	-
Is the sample size adequate for the study?	N=58, sufficient population size for pilot study	-
Selection criteria for subjects?	Selection criteria clearly detailed and were appropriate for study design and question	-
Appropriateness of study design to study question	Study design was appropriate to the study question	-
Were participants/care providers/outcome assessors blind to Laser Doppler Imaging images? If not, how could this affect the risk of bias?	Blind: Medical and nursing staff caring for the patients were unaware of results of Laser Doppler Imaging scans	-
Were there unexpected drop outs/exclusions during the study which were inadequately explained?	No reported withdrawals or exclusion	-
Is the choice of outcome measures appropriate to the study question?	Outcome measures described are appropriate	-
Were appropriate statistical analyses presented?	Sensitivity and specificity of both Laser Doppler Imaging and clinical assessments have been compared, this is sufficient to answer the study question	No other statistical analysis are reported
Quality of intervention with Laser Doppler Imaging – is scan timing appropriate?	Patients were scanned between 36 and 72 hours post burn, within the manufacturers recommended scan time	The manufacturer's recommended scan time is between 48 to 72 hours
Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination		

Niazi *et al.* (1997)		
Is the new Laser Doppler scanner a valuable adjunct in burn depth assessment?	**How is the question addressed in the study?**	**Comments by EAC**
Study type – cohort, observational, case studies.	Pilot study	Prospective pilot study
Is the sample size adequate for the study?	N=13, small sample size but considered adequate for pilot study no power analyses provided	-
Selection criteria for subjects?	Not adequately detailed	Only patients presented in the first part of the week
Appropriateness of study design to study question	Study design was entirely appropriate at the time of the pilot study	-
Were participants/care providers/outcome assessors blind to Laser Doppler Imaging images? If not, how could this affect the risk of bias?	No blinding according to methodology	-
Were there unexpected drop outs/exclusions during the study which were inadequately explained?	No – no exclusions or drop outs without inadequate explanation	No drop outs
Is the choice of outcome measures appropriate to the study question?	Yes all were appropriate to the study question	-
Were appropriate statistical analyses presented?	No statistical analyses detailed, but tables sufficiently indicate results for small data sample	-
Quality of intervention with Laser Doppler Imaging – is scan timing appropriate?	Patients were scanned at 24, 48 and 72 hours appropriate for this study question.	-
Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination		

La Hei *et al.* (2006)		
Can burn wound outcome, in a paediatric population be predicted by Laser Doppler Imaging in the absence of any direct clinical assessment?	**How is the question addressed in the study?**	**Comments by EAC**
Study type – cohort, observational, case studies.	Blinded audit	-
Is the sample size adequate for the study?	N=31 patients, 50 scans. Small sample size not adequate to answer study question	-
Selection criteria for subjects?	Yes sufficient details of this selection criteria have been provided	-
Appropriateness of study design to study question	Study design was appropriate considering the study question	-
Were participants/care providers/outcome assessors blind to Laser Doppler Imaging images? If not, how could this affect the risk of bias?	Reporters were blinded	Reporters were blinded and not involved with patients treatment and unaware of final burn outcome
Were there unexpected drop outs/exclusions during the study which were inadequately explained?	None	-
Is the choice of outcome measures appropriate to the study question?	Yes, outcome measures detailed were appropriate to the study question	-
Were appropriate statistical analyses presented?	Sensitivity and specificity reported but no other statistical data available	-
Quality of intervention with Laser Doppler Imaging – is scan timing appropriate?	Scans not all performed during the manufacturers recommended times.	Manufacturer recommends 48 to 72 hours post injury.
Centre for Reviews and Dissemination (2008) Systematic reviews. CRD's guidance for undertaking reviews in health care. York: Centre for Reviews and Dissemination		

4.1.4 Description and critique of manufacturers outcome selection

The outcomes addressed by the manufacturer submission are considered to be appropriate. Relevant outcomes, as outlined in the NICE scope and provided in the manufacturer submission are:

- prediction of healing time within 14 or 21 days
- treatment decision
- time to surgery
- length of hospital stay

For almost all of the clinical effectiveness studies, the primary outcome was the accuracy of the moorLDI2 in predicting healing time. In two studies the secondary outcomes were the assessment of the importance of other parameters, such as patient's age and gender and the burn cause, burn site and % TBSA, on LDI prediction of wound healing at 14 and 21 days. For most of the studies no secondary outcomes were reported. As previously stated, information regarding some of the outcomes (e.g. number of dressing changes, number of operations, wound complications) specified in the scope is not provided by the included clinical studies. Hence some outcomes specified in the NICE scope are not addressed.

The manufacturer states that the principal finding from the clinical evidence is that the moorLDI2 could aid the prediction of time to healing of a burn wound. It is also stated that in combination with clinical assessment, it enables earlier and more accurate predictions, which on average, result in a reduction in hospital stay of two to three days.

The EAC found that the evidence provided in the clinical effectiveness literature supports all these findings.

4.1.5 Describe and critique the statistical approach used

No statistical analysis was undertaken by the manufacturer, as systematic reviews and meta-analysis were not conducted on the grounds that it was inappropriate, with further details provided in Section 4.2.2. The EAC agrees that no statistical analysis and meta-analysis is feasible.

4.1.6 Summary statement about the review of clinical effectiveness

All the studies included in the submission investigated the ability of the moorLDI2 burn imager to assess wound depth and healing potential both in adult and paediatric patients. Most of the studies compared the results with clinical assessment and some with biopsy. All were relevant to the decision problem, in terms of patient populations and interventions, and the submitted evidence adequately reflects the decision problem. The relevant data from the included studies are reported in the submission document. However, even though not all relevant studies are included, it is anticipated that the manufacturer of the moorLDI2 is aware of these other studies.

The validity assessment of the included studies is adequate. The clinical outcomes selected for the assessment of moorLDI2 relate to those outlined in the NICE scope and the statistical methods undertaken within the included studies are adequately and appropriately reported.

4.2 Summary of submitted evidence

The clinical effectiveness evidence submitted by the manufacturer comprises 11 studies, as previously described (Section 4.1.2). The findings from the studies that are presented in the submission are summarised below.

4.2.1 Summary of results

Results from the included studies are presented in tabular form (page 60 and supplementary document) and described the accuracy of moorLDI2 in predicting healing time (sensitivity and specificity) and in facilitating earlier surgical decisions. The results are consistent with the evidence provided in the studies.

Accuracy of the moorLDI2 burn imager

The accuracy of moorLDI2 burn imager in the assessment of burn wounds in 8 studies was assessed with a variety of criteria, including accuracy to predict healing within 14 days or 21 days and by comparison with clinical and/or histological assessment of burn depth. The Hoeksema *et al.* study found that the LDI accuracy was 95% on day 3, which was significantly higher than the

clinical assessment (p<0.001) and 97.1% on day 5 (p=0.005). Jeng *et al.* found a 100% correlation between LDI and biopsy, in the Pape *et al.* study the accuracy was 97% and the agreement between biopsy and LDI was 100%

Sensitivity/specificity

In the Hoeksema *et al.* study the sensitivity was 100% and the specificity was 92.3%, Holand *et al.* sensitivity was 90% and specificity 96%, Pape *et al.* 100% and 95%, La Hei *et al.* 97% and 100% respectively on scan day 3 whereas in the Monstrey *et al.* study the LDI accuracy was reported as >90%

Surgical decisions

In two studies the use of LDI was related to earlier surgical decisions. The Kim *et al*. study found that the surgical decision was made three days earlier. In the Jeng *et al*. study it was two days.

Adverse events

There are no published adverse events associated with the LDI technology.

4.2.2 Critique of submitted evidence syntheses

The intervention is a medical device used for diagnostic purposes and not a treatment method for a specific condition. The studies included in the submission did not feature any randomised controlled trials; therefore the manufacturer submission does not undertake meta-analysis or systematic reviews. The EAC agrees that a meta-analysis is not feasible.

The submission provides a summary of clinical findings in relation to the accuracy of the moorLDI2 in the assessment of burn wounds in terms of the sensitivity and specificity, the positive and negative predictive values and the time to surgical decision. Tables are used to compare accuracy across the different studies (pages 59 to 60 and supplementary document), which also correctly include the different patient populations.

5 Assessment of cost analysis

5.1 Overview of manufacturer's economic assessment

5.1.1 Methods

This section assesses the cost analysis submitted by the manufacturer regarding the use of moorLDI2 for the assessment of intermediate depth burn wounds. The manufacturer submission includes:

- A description of the literature search that was undertaken for the identification of cost and cost effectiveness studies in relation to the moorLDI2
- A report of the *de novo* cost analysis that was conducted, including the patient population, model structure, model parameters, assumptions, data sources and sensitivity analyses
- A summary of variables applied in the economic model
- An Excel file showing the base case results and some sensitivity analyses
- An Excel file containing additional information regarding model parameters

A summary of the relevant areas of the submission document for the cost analysis is shown in Table 2.

Table 2: Summary of key information for cost analysis

	Reference in submission document	Key tables/figures in submission document
Review of literature	p 67, 68, 78, 79 and 113 to 121 (Appendix 6 to 9)	Table p 79
Model structure	p 68, 69	-
Transition probabilities	p 71 to 75	Table B9
Time horizon	p 69	Table B8
Adverse events	p 83	-
Resource use and costs	p 76 to 82	Table p 77, Table B10, Table B11
Sensitivity analysis	p 84 to 89	-
Results	p 85 to 89	-

Identification of studies

The search strategy for cost-effectiveness studies is reported in Appendix 6: Search strategy for cost-effectiveness and cost studies (section 6.1), pages 113-115. The submission includes a search of the NHS EED (via CRD Database search engine) but it does not include a search in Medline, Embase or EconLIT.

The search strategy presented in the submission is considered appropriate but is inadequately reported. There is a lack of detail in the description of the manufacturer's searches for the studies. The submission does not include the search strategy applied for each different database and the EAC assumed that the same strategy (as described in Appendix 6) was applied in all searched databases.

The terms used in the search strategy presented in the submission are considered to be appropriate, even though not extensive. The use of such a search has the risk of missing relevant studies. Terms such as 'cost-effectiveness' and 'cost-benefit' could also be used as additional search terms. The EAC also noted the absence of the use of any subject index headings (for example, MeSH).

There is no indication that any limits were applied to the search strategy.

The search strategy for costs reported in Appendix 8: Search strategy for Section 6.4 (Measurement and Validation of health effects) suffers from the same issues as above.

The manufacturer submission states that no relevant studies were identified in any of their searches. The EAC agrees that there is no published economic evaluation for the use of moorLDI2 technology in the assessment of burn wounds. However, the three already mentioned reviews by Hemington-Gorse (2005), Mandal (2006) and Sainsbury (2008), which assessed the clinimetrics of LDI also have comments on the cost of the technology. The EAC is confident that the manufacturer is aware of these reviews as some of them were used to provide data for the cost analysis. However, details of their

identification are not provided in the literature search. The studies used by the manufacturer in the cost analysis model can be found in Appendix Two.

Model structure

A *de novo* cost analysis was conducted by the manufacturer to assess the cost savings to the NHS of the introduction of the LDI technology for the assessment of burn wounds of an indeterminate depth. The model is presented in the submission as an executable Excel file, which is considered appropriate by the EAC. Patients used in the model were patients admitted to burn centres and who were clinically assessed to have, or to possibly have, one or more intermediate burns.

As there is a lack of cost analysis studies no formal model structure could be considered. The savings generated by reduced length of hospital stay and fewer operations were calculated per patient by a bottom-up approach. The length of the operation was also considered in the calculations on the spreadsheets attached to the submission. The period of hospitalisation (seven to eight days) is taken as the time horizon of the model as the main benefits of LDI in terms of resource savings are expected to be during this initial period.

No comparator was used in this model, which is considered to be an appropriate approach by the EAC.

Health States

The manufacturer states that, as this is a diagnostic tool, there are no changes in the patients' health state due to the use of the moorLDI2 so there are no relevant health state changes to consider.

Assumptions

A list of all assumptions in the *de novo* economic model is provided in the submission (page 76). The manufacturer states that these assumptions are justified throughout the submission and the cost analysis spreadsheet.

Data sources

The main sources of data for the model were the Unit cost of Health and Social Care 2009, consultations with users and a number of studies, i.e. Hemington-Gorse *et al* (2009), Pape *et al* (2001), Griffiths *et al.* and Enoch *et al* (2009).

Resources and costs

The costs included in the model are based on the costs for non-elective treatment of patients with burn injuries requiring hospitalisation. These costs, taken from the manufacturer submission, are presented in Table 3 andTable 4

Table 3: Cost and resource implications to the NHS

Parameter	Range	Typical
Number of moorLDI2 systems	25 to 64	28*
Leasing cost	-	£22,000
Purchasing cost	-	£50,000
Servicing cost	-	£8,000
Nurse operation time (min)	30 to 90 min	60
Nurse hourly rate	-	£45
Clinician interpretation time (min)	5 to30 min	15
Clinician hourly rate	-	£170
Registrar hourly rate	-	£61
Administration cost	-	£15
NHS staff training cost	-	£3,416

Note: * When the EAC ran the model for adult and paediatric centres, 5 moorLDI2 systems were used.

Table 4: Cost benefits

Parameter	Range	Base case
Number of patients admitted	8,000-16,000	10,000
Percentage of patients scanned	10%-100%	70%*
Percentage of adults scanned	60%-90%	60%
Percentage of children scanned	10%-40%	40%
Number of bed days saved	2-3 days	2*
Percentage of operations saved	10%-30%	17%
Average time of operation	1-4 hours	1*
Cost of day bed adult	£320-£772	£378
Cost of day bed child	£320-£794	£794
Cost of operation per hour	£3000-£5000	£4,593

* Variation of these values was addressed in the manufacturer scenarios.

All of these figures are supported by the literature referred to in the manufacturer's spreadsheet. However, the EAC considered the hourly rate for operating theatres to be too high (£4,593; the figure used by the manufacturer, is supported by the literature (Hemington-Gorse *et al*. 2009)) and, in consultation with the NICE expert advisers, a lower figure of £2,043 was derived and applied to be used as part of the additional EAC case scenarios (Appendix Four).

The National Schedule of Reference Costs Year 2008-2009 - NHS Trusts Non-Elective Inpatient (Long Stay) HRG Data is presented in the manufacturer submission (page 77). The cost for a standard bed and an average of seven to eight days length of stay in the hospital were used.

No adverse events resulting from the use of Moor Instruments laser Doppler imagers were reported and hence no adverse events costs were taken into account.

Transition probabilities

The manufacturer states that as no formal model structure has been considered, there are no health states to transition between and therefore transition probabilities were not required (page 71).

Time horizon

The period of hospitalisation (seven to eight days) was used as the time horizon for the analysis. There was no extrapolation of results beyond this period as the main benefits of laser Doppler imaging in terms of resource savings are expected to be during the initial stay in hospital. Other secondary benefits such as reduced healing time after grafting and less dressing required, fall outside of this time frame and are much harder to quantify.

Discounting

No discounting is considered by the manufacturer in the submission.

Sensitivity analysis

A deterministic sensitivity analysis was undertaken. The manufacturer submission states that a probabilistic sensitivity analysis was not possible to

be conducted as no appropriate formal model could be identified and therefore none was used. The following parameters were investigated using sensitivity analysis:

- percentage of patients admitted and scanned by moorLDI2
- number of bed days saved
- average operation time saved

Six scenarios with varying values for both lease and purchase options are presented and are considered realistic by the EAC (Appendix 3).

The EAC further considered a number of additional scenarios which are presented in Appendix Four. In each case the use of the moorLDI2 is supported by potential savings to the NHS.

5.1.2 Results

Results are presented in terms of costs savings per patient scanned and net cost savings to the NHS for both leasing and purchasing options. Overall costs to the NHS of using the moorLDI2 technology for burn assessment, for one and five years are also reported, in addition to the breakdown of costs associated with the technology, service, administration, staff training and operation costs.

There are five additional scenarios undertaken by the manufacturer that are presented in the sensitivity analysis along side the base case. A full description of the results is shown in the included submission spreadsheet. The EAC has included selected results in Appendix Three: Cost model results

5.1.3 Model validation

The submission states that the cost model is based on savings arising from reduced bed days, operations avoided and operation time saved, against the cost to the NHS of either leasing or purchasing the moorLDI2. The validation is based on published results from studies performed by a number of burn surgeons for a period of more than 10 years. However, it is not reported whether the model structure has been validated by clinical experts.

5.2 Critique of approach used

The manufacturer has spread the cost of purchasing the moorLDI2 units over five years. The service cost per year was added to the purchasing option; the service costs were included within the lease option.

The training costs to the NHS have been spread over two years; this was considered appropriate allowing for the turnover of staff within the NHS.

All the figures used by the manufacturer are supported either by the literature or consultation and all are considered appropriate by the EAC except for the hourly rate for saved theatre time which the EAC considered to be too high.

A comparative cost analysis of the use of moorLDI2 together with clinical assessment and the use of clinical assessment alone for decision making in the treatment of burn wounds was the scope of the cost analysis issued by NICE. The manufacturer submission conducted an analysis of costs savings to the NHS (in a total of 28 burn centres) where the moorLDI2 was used for assessment of burn wounds. No comparator was used in this analysis which was considered appropriate by the EAC.

In summary, the EAC considers the model to be accurate and simple to use giving reliably consistent answers, which reflects real world cases.

5.3 Results included in manufacturer's submission

The results of the cost model are presented in the cost analysis spreadsheet; the results of the best case and worst case scenarios are also reported on in the submission document (page 89). The submitted cost analysis spreadsheet presents six scenarios which are included in the manufacturer's sensitivity analysis.

The cost saving per patient scanned ranges for the worst to the best case scenario from £1,055 to £4,583 for the leasing option and from £1,167 to £4,594 for the purchasing option. The net cost saving to the NHS per year ranges from £1,055,462 to £45,827,752 for the leasing option and from £1,167,462 to £45,939,752 for the purchasing option.

For the base case scenario, ((Scenario 1 Typical) 70% of patients scanned with 2 days saving in bed days and 1 hour saving of operation time) the breakeven point for the NHS as a whole (28 centres) is 576 admitted patients or 403 scanned patients for the leasing option. This translates into 21 patients admitted or 14 patients scanned per centre. For the purchasing option the breakeven point for the NHS is 485 admitted patients or 340 scanned patients. This converts into 17 admitted patients or 12 scanned patients per centre.

The costing to the NHS is also calculated, and ranges from £814,148 to £1,736,648 for one year and from £4,070,740 to £8,683,240 for five years for the leasing option. For the purchasing option the costing ranges from £702,148 to £1,624,648 for one year and from £3,510,740 to £8,123,240 for five years.

The results from the submission are summarised in tables 5, 6, 7and 8 below. The scenarios are described in Appendix Three.

Table 5: Net cost saving per patient (Leasing)

Scenario	Cost Saving	Cost Saving per patient scanned	Cost to NHS (Leasing Option)	Net Cost Saving	Net Cost Saving per patient scanned
Scenario 1	£13,087,270	£1,870	£1,429,148	£11,658,122	£1,665
Scenario 2	£47,564,400	£4,756	£1,736,648	£45,827,752	£4,583
Scenario 3	£1 ,869,610	£1,870	£814,148	£1,055,462	£1,055
Scenario 4	£16,898,070	£2,414	£1,429,148	£15,468,922	£2,210
Scenario 5	£29,484,280	£4,212	£1,429,148	£28,055,132	£4,008
Scenario 6	£33,295,080	£4,756	£1,429,148	£31,865,932	£4,552

Table 6: Net cost saving per patient (Purchasing)

Scenario	Cost Saving	Cost Saving per patient scanned	Cost to NHS (Purchasing Option)	Net Cost Saving	Net Cost Saving per patient scanned
Scenario 1	**£13,087,270**	**£1,870**	**£1,317,148**	**£11,770,122**	**£1,681**
Scenario 2	**£47,564,400**	**£4,756**	**£1,624,648**	**£45,939,752**	**£4,594**
Scenario 3	**£1,869,610**	**£1,870**	**£702,148**	**£1,167,462**	**£ 1,167**
Scenario 4	**£16,898,070**	**£2,414**	**£1,317,148**	**£15,580,922**	**£ 2,226**
Scenario 5	**£29,484,280**	**£4,212**	**£1,317,148**	**£28,167,132**	**£4,024**
Scenario 6	**£33,295,080**	**£4,756**	**£1,317,148**	**£31,977,932**	**£4,568**

Table 7: Cost to NHS (Leasing)

Scenario	Number of patients scanned	1 Year Cost to NHS	5 Years Cost to NHS
Scenario 1	7,000	£1,429,148	£7,145,740
Scenario 2	10,000	£1,736,648	£8,683,240
Scenario 3	1,000	£814,148	£4,070,740
Scenario 4	7,000	£1,429,148	£7,145,740
Scenario 5	7,000	£1,429,148	£7,145,740
Scenario 6	7,000	£ 1,429,148	£7,145,740

Table 8: Cost to NHS (Purchasing)

Scenario	Number of patients scanned	1 Year Cost to NHS	5 Years Cost to NHS
Scenario 1	7,000	£1,317,148	£6,585,740
Scenario 2	10,000	£1,624,648	£8,123,240
Scenario 3	1,000	£702,148	£3,510,740
Scenario 4	7,000	£1,317,148	£6,585,740
Scenario 5	7,000	£1,317,148	£6,585,740
Scenario 6	7,000	£1,317,148	£6,585,740

Table 9 shows the comparison of the six scenarios submitted by the manufacturer plus the four scenarios (*shown in italics*) run by the EAC against the base case, for both the leasing and purchasing option, of the saving per patient scanned.

Table 9: Cost saving per patient scanned

Scenario	Lease option	Purchase option
Base Case (Scenario 1)	**1665**	**1681**
100% patients scanned 3 bed days and 2 operation hours saved	4583	4594
10% patients scanned 2 bed days and 1operation hour saved	1055	1167
Base case with 3 bed days saved	2210	2226
Base case with 2 bed days and 2 operation hours saved	4008	4024
Base case with 3 bed days and 2 operation hours saved	4552	4568
Base case with £2043 per operation hour saved	1232	1248
Base case with 30% patients scanned	1208	1246
*Base case with 2000 adult patients, five centres**	1344*	1358*
*Base case with 2000 paediatric patients, five centres**	2176*	2190*

Note: * these cases were included as several of the UK burns units specialise in either adult or paediatrics patents

The overall range of cost saving to the NHS per patient scanned is from £1055 for the leasing option to £4594 for the purchasing option.

Table 10 shows the comparison of the six manufacturer's scenarios plus the four scenarios (*shown in italics*) run by the EAC against the base case for both the leasing and purchasing option of the number of patients required for the breakeven point. The numbers in parenthesis are the number of patients which need to present at each burns centre to achieve the breakeven point.

Table 10: Breakeven point based on number of patients presenting.

Scenario	Lease option	Purchase option
Base Case (Scenario 1)	**576 (21)**	**485 (17)**
100% patients scanned 3 bed days and 2 operation hours saved	231 (9)	194 (7)
10% patients scanned 2 bed days and one operation hour saved	4028 (144)	3394 (122)
Base case with 3 bed days saved	440 (16)	371 (14)
Base case with 2 bed days and 2 operation hours saved	399 (15)	337 (12)
Base case with 3 bed days and 2 operation hours saved	329 (12)	277 (10)
Base case with £2043 per operation hour saved	763 (28)	643 (23)
Base case with 30% patients scanned	1641 (59)	1383 (50)
*Base case with 2000 adult patients, five centres**	127 (26)*	107 (22)*
*Base case with 2000 paediatric patients , five centres**	80 (16)*	68 (14)*

Note: * these cases were included as several of the UK burns units specialise in either adult or paediatric patients.

As can be seen the breakeven point for leasing the moorLDI2 ranges from 9 to 144 patients and for purchasing ranges from 7 to 122 patients, with the base case being 21patients for leasing and 17 patients for purchasing.

5.4 Comment on validity of results presented with reference to methodology used

The results reported in the manufacturer submission (page 89) indicate that the moorLDI2 is likely to give cost savings across each of the six scenarios as presented by the manufacturer in the spreadsheet (Appendix Three). The moorLDI2 was also found to be cost effective across the additional scenarios run by the EAC (Appendix Four).

The EAC agrees that scenario 1 is a realistic base case. However, scenario 3, the worst case at 10% of patients scanned, is considered to be below a reasonable percentage of patients scanned.

The EAC validated the manufacturer's cost model (Excel spreadsheet) and input values as far as possible in the associated time constraints. The methodology behind the model and construction of the model are not fully explained within the submission. However, the model is straightforward and the scenarios appeared to be sensible.

The reliance on data from Hemington-Gorse *et al* for hourly cost of an operation may be considered a weakness, but given the lack of economic studies identified in the literature search this is acceptable.

5.5 Summary of uncertainties and issues

The EAC considered the manufacturer submission in relation to the cost impact of moorLDI2 to be adequate in addressing the decision problem. Sensitivity analysis was conducted in order to explore the robustness of the results to changes in various parameters. The main issues raised by the EAC are summarised below.

Literature searches

The search strategies provided in the submission are not adequately reported; therefore the EAC is not confident about the identification of studies and whether all relevant studies were included in the submission.

Data source

The main sources of data for the model are the Unit cost of Health and Social Care 2009, consultations with users and four studies i.e. Hemington-Gorse *et al*(2009), Pape *et al* (2001), Griffiths *et al.* and Enoch *et al* (2009).
There is an uncertainty whether the operating theatre costs (£4593) is appropriate (this was supported by the literature) and a lower cost of £2043 per hour was arrived in consultation with the NICE expert advisers.

Execution of the model

Details of the model are inadequately reported in the submission. However, the model is simple to execute and appears to give reliable results which are repeatable.

Adverse events

No adverse events resulting from the use of a Moor Instruments Ltd LDI were reported and hence no adverse events costs were taken into account.

Additional work undertaken by the External Assessment Centre

Additional work undertaken by the EAC comprised:

- additional literature searches in order to investigate the reliability of the manufacturer's literature searches that were used to identify the clinical effectiveness of the intervention
- comments have been provided alongside the manufacturer's critical appraisal of the included clinical effectiveness studies
- additional sensitivity analyses have been undertaken
- cost modelling was undertaken for adult only and for paediatric only burn units, using the manufacturer's cost analysis executable spreadsheet
- the operating theatre cost per hour was calculated outside of the manufacturer's submission

6 Discussion

6.1 Summary of clinical effectiveness issues

The literature search for clinical effectiveness, even though not adequately reported in the submission, is appropriate and identifies the majority of relevant studies. The 11 studies included in the submission comprise two non-randomised studies, five observational studies, one clinical trial, two audits and one statistical analysis; all are related to burn wound assessment using the moorLDI2 burn imager.

The included studies were all conducted in burn centres in UK and worldwide. The studies were focused on the assessment of intermediate depth burn wound using the laser Doppler imager. The accuracy of the moorLDI2 in assessing the depth of the burn and predict healing time was compared in the majority of the studies to that of the clinical assessment.

The outcomes addressed by the submission are considered appropriate and relevant and include the accuracy of moorLDI2 in predicting healing time within 14 to 21 days, length of hospital stay and decision to grafting. All these outcomes were outlined in the NICE scope.

The EAC identified a number of additional studies that are not included in the manufacturer submission although some are listed in their bibliography. However, none of these studies contradict the outcomes of the studies included in the manufacturer submission and, in general, support the use of moorLDI2 for the assessment of burn wounds.

6.2 Summary of cost issues

As with the clinical effectiveness, the cost literature searches were not extensive and are inadequately reported in the submission. Although no studies are identified by the manufacturer, the data of a number of studies are used in the cost analysis model.

The submitted cost analysis presents six scenarios which are considered to be appropriate. All the cost data used by the manufacturer is supported by evidence, however the operating theatre rates were considered to be high.

The base case analysis demonstrated that the cost saving to the NHS per year is £11,658,122 for the leasing option and £11,770,122 for the purchasing option. This is translated to a saving of £1,665 per patient scanned for the leasing option and £1,681 for the purchasing option. The sensitivity analysis identified the key driver of the results to be the number of patients scanned. Other influential parameters such as operating time and bed days were also investigated.

6.3 Implications for guidance and research

There are two additional potential costs savings identified from the use of moorLDI2 which fall outside the time horizon of the submission but may merit further research.

- the reduced need for prophylactic anti-scar therapy when wounds have healed where surgery has been avoided when the moorLDI2 is used
- the use of the moorLDI2 in earlier indication of whether there is adequate or poor vascular in-growth post grafting deep or full thickness burn wounds and the reduction in the length of hospital stay

Appendix One: Relevant studies identified by the EAC not included in the manufacturer's clinical effectiveness literature

- Jaskille *et al.* (2010) Critical Review of Burn Depth Assessment Techniques: Part II. Review of Laser Doppler Technology. Journal of Burn Care & Research 31 (1): 151-157

- Nguyen *et al.* (2010) Laser Doppler Imaging prediction of burn wound outcome in children: Is it possible before 48 hours. Burns 36: 793-798

- Holland *et al.* (2007) The Influence of Burn Wound Dressings on Laser Doppler Imaging Assessment of a Standardised Cutaneous Injury Model. Journal of Burn Care & Research 28: 871–878

- Wang *et al.* (2010) Ultrasound assessed thickness of burn scars in association with laser Doppler imaging determined depth of burns in paediatric patients. Burns in press. Accessed on line 06/09/2010.

- Hemington-Gorse S.J.(2009). A comparison of laser Doppler imaging with other measurement techniques to assess burn depth. J Wound Care. 14 (4): 151-153

- Mandal (2006) Burn wound depth assessment-is laser Doppler imaging the best measurement tool available? International Wound Journal 3 (2): 138-143

- Sainsbury D.C.G. (2008) Clinical evaluation of the clinimetrics of laser Doppler imaging n burn assessment. Journal of Wound Care, Vol17, No. 5 193-200

Appendix Two: Studies used to provide cost analysis data not identified by the manufacturer's literature searches for cost analysis

- Hemington-Gorse *et al* (2009). Burn care costing: The Welsh experience. Burns 35 378-382

- Griffiths *et al.* (2006).The cost of a hot drink scald. Burns 32 (2006) 372–374

- Enoch *et al* (2009). Emergency and early management of burns and scalds. BMJ. 8: 338: b1037

Appendix Three: Manufacturer's Cost Model results

The in depth results of the six scenarios (extracted) from the manufacturer's executable cost analysis spreadsheet, run by the EAC to verify the feasibility of the NHS adopting this technology are shown below.

Table 11: Manufacturer's scenarios

Scenario No	Description
Scenario 1 (Typical)	Assume 70% of patients admitted will be scanned by moorLDI, number of bed days of 2 days, and average operation time of 1 hour
Scenario 2 (Highest saving)	Assume all patients admitted will be scanned by moorLDI, number of bed days of 3 days, and average operation time of 2 hour
Scenario 3 (Lowest Saving)	Assume 10% of patients admitted will be scanned by moorLDI, number of bed days of 2 days, and average operation time of 1 hour
Scenario 4	Assume 70% of patients admitted will be scanned by moorLDI, number of bed days of 3 days, and average operation time of 1 hour
Scenario 5	Assume 70% of patients admitted will be scanned by moorLDI, number of bed days of 2 days, and average operation time of 2 hour
Scenario 6	Assume 70% of patients admitted will be scanned by moorLDI, number of bed days of 3 days, and average operation time of 2 hour

As shown the parameters that the manufacturer investigated by sensitivity analysis were:

Percentage of patients scanned (10, 70 100%).

Bed days saved (2 or 3)

Operation time saved 1 or 2 hours

The EAC feels that Scenario 1 is realistic and is supported by the clinical literature.

None of the manufacturer scenarios included inflation or discount.

Table 12: Cost Saving

Scenario	Percentage of patients scanned	Number of patients scanned	Number of adults scanned	Number of children scanned	Number of bed days saved	Number of operations saved	Average time of operation	Cost of day bed adult	Cost of day bed child	Cost of operation	Cost Saving
Scenario 1	70%	7,000	4,200	2,800	2	1,190	1	£378	£794	£4,593	**£13,087,270**
Scenario 2	100%	10,000	6,000	4,000	3	1,700	2	£378	£794	£9,186	**£47,564,400**
Scenario 3	10%	1,000	600	400	2	170	1	£378	£794	£4,593	**£1,869,610**
Scenario 4	70%	7,000	4,200	2,800	3	1,190	1	£378	£794	£4,593	**£16,898,070**
Scenario 5	70%	7,000	4,200	2,800	2	1,190	2	£ 378	£794	£9,186	**£29,484,280**
Scenario 6	70%	7,000	4,200	2,800	3	1,190	2	£ 378	£794	£9,186	**£33,295,080**

Table 13: Cost to NHS (Leasing)

Scenario	Percentage of patients scanned	Number of patients scanned	Total Leases	Total NHS staff training cost	Total Nurse operation cost#	Total Clinician cost	Total Admin cost	1 Year Cost to NHS	5 Years Cost to NHS
Scenario 1	70%	7,000	£616,000	£ 95,648	£315,000	£297,500	£105,000	**£1,429,148**	**£7,145,740**
Scenario 2	100%	10,000	£616,000	£ 95,648	£450,000	£425,000	£150,000	**£1,736,648**	**£8,683,240**
Scenario 3	10%	1,000	£616,000	£ 95,648	£45,000	£ 42,500	£ 15,000	**£814,148**	**£4,070,740**
Scenario 4	70%	7,000	£616,000	£ 95,648	£315,000	£297,500	£ 105,000	**£1,429,148**	**£7,145,740**
Scenario 5	70%	7,000	£616,000	£95,648	£315,000	£297,500	£ 105,000	**£1,429,148**	**£7,145,740**
Scenario 6	70%	7,000	£616,000	£95,648	£315,000	£297,500	£ 05,000	**£ 1,429,148**	**£7,145,740**

Note: This model assumes 28 moorLDI units leased at £22.000 (includes servicing)

Table 14: Cost to NHS (Purchasing)

Scenario	Percentage of patients scanned	Number of patients scanned	Total purchasing cost	Total service cost	Total NHS staff training cost	Total Nurse operation cost	Total Clinician cost	Total Admin cost	1 Year Cost to NHS	5 Years Cost to NHS
Scenario 1	70%	7,000	£1,400,000	£224,000	£95,648	£315,000	£297,500	£105,000	**£1,317,148**	**£6,585,740**
Scenario 2	100%	10,000	£1,400,000	£224,000	£95,648	£450,000	£425,000	£150,000	**£1,624,648**	**£8,123,240**
Scenario 3	10%	1,000	£1,400,000	£224,000	£95,648	£45,000	£ 42,500	£15,000	**£702,148**	**£3,510,740**

Scenario 4	70%	7,000	£1,400,000	£224,000	£95,648	£315,000	£297,500	£105,000	**£1,317,148**	**£6,585,740**
Scenario 5	70%	7,000	£1,400,000	£224,000	£95,648	£315,000	£297,500	£105,000	**£1,317,148**	**£6,585,740**
Scenario 6	70%	7,000	£1,400,000	£224,000	£95,648	£315,000	£297,500	£105,000	**£1,317,148**	**£6,585,740**

Note: this model assumes 28 moorLDI purchased at £50,000 plus £8,000 per year service.

Table 15: Table: Net cost saving (Leasing)

Scenario	Percentage of patients scanned	Number of bed days saved	Average time of operation	Cost Saving	Cost Saving per patient scanned	Cost to NHS (Leasing Option)	Net Cost Saving	Net Cost Saving per patient scanned
Scenario 1	70%	2	1	**£13,087,270**	**£1,870**	**£1,429,148**	**£11,658,122**	**£1,665**
Scenario 2	100%	3	2	**£47,564,400**	**£4,756**	**£1,736,648**	**£45,827,752**	**£4,583**
Scenario 3	10%	2	1	**£1 ,869,610**	**£1,870**	**£814,148**	**£1,055,462**	**£1,055**
Scenario 4	70%	3	1	**£16,898,070**	**£2,414**	**£1,429,148**	**£15,468,922**	**£2,210**
Scenario 5	70%	2	2	**£29,484,280**	**£4,212**	**£1,429,148**	**£28,055,132**	**£4,008**
Scenario 6	70%	3	2	**£33,295,080**	**£4,756**	**£1,429,148**	**£31,865,932**	**£4,552**

Table 16: Table: Net cost saving (Purchasing)

Scenario	Percentage of patients scanned	Number of bed days saved	Average time of operation saved	Cost Saving	Cost Saving per patient scanned	Cost to NHS (Purchasing Option)	Net Cost Saving	Net Cost Saving per patient scanned
Scenario 1	70%	2	1	**£13,087,270**	**£ 1,870**	**£1,317,148**	**£11,770,122**	**£1,681**
Scenario 2	100%	3	2	**£47,564,400**	**£4,756**	**£1,624,648**	**£45,939,752**	**£4,594**
Scenario 3	10%	2	1	**£1,869,610**	**£1,870**	**£702,148**	**£1,167,462**	**£ 1,167**
Scenario 4	70%	3	1	**£16,898,070**	**£2,414**	**£1,317,148**	**£15,580,922**	**£ 2,226**
Scenario 5	70%	2	2	**£29,484,280**	**£4,212**	**£1,317,148**	**£28,167,132**	**£4,024**
Scenario 6	70%	3	2	**£33,295,080**	**£4,756**	**£1,317,148**	**£31,977,932**	**£4,568**

The range of saving to the NHS per patient scanned varies from £1055 (for the lease option if only 10% of patients are scanned), up to £4594 (for the purchase option if 100% of patients are scanned).

Option1 Leasing: Breakeven point for NHS as a whole (28 burn centres identified) is 576 patients admitted with 70% scanned or 403 patients scanned; for each burn centre identified, the breakeven point is 21 patients admitted or 14 patients scanned.

Option2 Purchasing: Breakeven point for NHS as a whole (28 burn centres identified) is 485 patients admitted with 70% scanned or 340 patients scanned; for each burn centre identified, the breakeven point is 17 patients admitted or 12 patients scanned.

Appendix Four: EAC Cost Model results.

It was considered that the hourly rate for operating theatres used by the manufacturer was too high and, in consultation with the NICE expert advisers, a lower rate was derived (Table 17) and applied to be used as part of additional EAC case scenarios

Table 17: Hourly cost of theatre time including staff

Resource	Cost	Total cost
Consultants anaesthetic (1) surgical (1)	£170* per hour	£340
Registrar anaesthetic (1) & surgical (1)	£61* per hour	£121
Nurses anaesthetic (1) & surgical (2)	£45* per hour	£135
Healthcare assistant (1)	£16* per hour	£16
Empty theatre	£993**	£1430
Hourly cost of theatre with staff		£2043

*Unit cost of Health and Social Care 2009
** Griffiths *et al*. 2006 (plus 20% + 20%)

The EAC undertook additional sensitivity analyses using the scenarios in Table 18 which are presented here

Table 18: EAC scenarios

Scenario No	Description
Scenario 7 Low theatre costs	Assume 70% of patients admitted will be scanned by moorLDI, number of bed days of 2 days, and average operation time of 1 hour
Scenario 8	Assume 30% of patients admitted will be scanned by moorLDI, number of bed days of 2 days, and average operation time of 1 hour
Scenario 9 Adult patients	Assume 70% of 2000 adult patients admitted will be scanned at five sites, number of bed days of 2 days, and average operation time of 1 hour
Scenario 10 Paediatric patients	Assume 70% of 2000 paediatric patients admitted will be scanned at five sites, number of bed days of 2 days, and average operation time of 1 hour

Scenario 9 and10 were undertaken as a number of burns units specialise in either adult or paediatric patients, so would not treat the same ratio of 60% adult patients and 40% paediatric patients. A lower number of patients (2,000) was derived based on only 5 moorLDI2 units not the 28 for the NHS as a whole.

Table 19: Net cost saving (Leasing)

Scenario	Number of patients admitted	% of patients scanned	Number of bed days saved	Average time of operation	Cost Saving	Cost Saving per patient scanned	Cost to NHS (Leasing Option)	Net Cost Saving	Net Cost Saving per patient scanned
Scenario 7	10,000	70%	2	1	**£10,052,770**	**£1,436**	**£1,429,148**	**£8,623,622**	**£1,232**
Scenario 8	10,000	30%	2	1	**£4,644,300**	**£1,548**	**£1,019,148**	**£3,625,152**	**£1,208**
Scenario 9	2,000	70%	2	1	**£2,151,534**	**£1,537**	**£270,580**	**£1,880,954**	**£1,344**
Scenario 10	2,000	70%	2	1	**£3,316,334**	**£2,369**	**£270,580**	**£3,045,754**	**£2,176**

Table 20: Net cost saving (Purchasing)

Scenario	Number of patients admitted	% of patients scanned	Number of bed days saved	Average time of operation	Cost Saving	Cost Saving per patient scanned	Cost to NHS (Purchasing Option)	Net Cost Saving	Net Cost Saving per patient scanned
Scenario 7	10,000	70%	2	1	**£10,052,770**	**£1,436**	**£1,317,148**	**£8,735,622**	**£1,248**
Scenario 8	10,000	30%	2	1	**£4,644,300**	**£1,548**	**£907,148**	**£3,737,152**	**£1,246**
Scenario 9	2,000	70%	2	1	**£2,151,534**	**£1,537**	**£250,580**	**£1,900,954**	**£1,358**
Scenario 10	2,000	70%	2	1	**£3,316,334**	**£2,369**	**£250,580**	**£3,065,754**	**£2,190**

Table 21: NHS cost (Leasing)

Scenario	Number of patients admitted	% of patients scanned	Number of patients scanned	Number of LDIs	Total leasing cost	Total NHS staff training cost	Total Nurse operation cost	Total Clinician cost	Total Admin cost	1 Year Cost to NHS	5 Years Cost to NHS
Scenario 7	10,000	70%	7,000	28	£616,000	£95,648	£315,000	£297,500	£105,000	**£1,429,148**	**£7,145,740**
Scenario 8	10,000	30%	3,000	28	£616,000	£95,648	£135,000	£127,500	£45,000	**£1,019,148**	**£5,258,804**
Scenario 9	2,000	70%	1,400	5	£110,000	£17,080	£63,000	£59,500	£21,000	**£270,580**	**£1,352,900**
Scenario 10	2,000	70%	1,400	5	£110,000	£17,080	£63,000	£59,500	£21,000	**£270,580**	**£1,352,900**

Table 22: NHS cost (Purchasing)

Scenario	Number of patients admitted	% of patients scanned	Number of patients scanned	Number of LDIs	Total purchasing cost	Total service cost	Total NHS staff training cost	Total Nurse operation cost	Total Clinician cost	Total Admin cost	1 Year Cost to NHS	5 Years Cost to NHS
Scenario 7	10,000	70%	7,000	28	£1,400,000	£224,000	£95,648	£315,000	£297,500	£105,000	**£1,317,148**	**£6,585,740**
Scenario 8	10,000	30%	3,000	28	£1,400,000	£224,000	£95,648	£135,000	£127,500	£45,000	**£907,148**	**£4,636,084**
Scenario 9	2,000	70%	1,400	5	£250,000	£40,000	£17,080	£63,000	£59,500	£21,000	**£250,580**	**£1,252,900**
Scenario 10	2,00	70%	1,400	5	£250,000	£40,000	£17,080	£63,000	£59,500	£21,000	**£250,580**	**£1,252,900**