NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Procedure Name:	**Mechanical clot retrieval for treating acute ischaemic stroke (1026/2)**
Name of Specialist Advisor:	**Dr Ajay Bhalla**
Specialist Society:	**British Association of Stroke Physicians (BASP)**
Please complete and return to:	azeem.madari@nice.org.uk OR sally.compton@nice.org.uk

1 Do you have adequate knowledge of this procedure to provide advice?

X☐ Yes.

☐ No – please return the form/answer no more questions.

1.1 Does the title used above describe the procedure adequately?

☐ Yes.

☐ No. If no, please enter any other titles below.

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

X☐ Yes.

☐ Is there any kind of inter-specialty controversy over the procedure?

☐ No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:

The next two questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure please answer question 2.2.2.

2.2.1 If you are in a specialty which does this procedure, please indicate your experience with it:

X☐ I have never performed this procedure.

☐ I have performed this procedure at least once.

☐ I perform this procedure regularly.

Comments:

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☐ I have never taken part in the selection or referral of a patient for this procedure.

X☐ I have taken part in patient selection or referred a patient for this procedure at least once.

☐ I take part in patient selection or refer patients for this procedure regularly.

Comments:

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

x☐ I have undertaken bibliographic research on this procedure.

☐ I have undertaken research on this procedure in laboratory settings (e.g. device-related research).

☐ I have undertaken clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

☐ Other (please comment)

Comments:

I have written review articles on this procedure and BASP society standards

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

☐ Established practice and no longer new.

X☐ A minor variation on an existing procedure, which is unlikely to alter that procedure's safety and efficacy.

☐ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

ESTABLISHED PRACTICE (EVIDENCE BASED) BUT LIMITED UPTAKE OF PROCEDURE NATIONALLY

3.2 What would be the comparator (standard practice) to this procedure?

THROMBOLYSIS WITH TISSUE PLASMINOGEN ACTIVATOR

3.3 Please estimate the proportion of doctors in your specialty who are performing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

X☐ Fewer than 10% of specialists engaged in this area of work.

☐ Cannot give an estimate.

Comments:

Procedure undertaken by neuro-interventional radiologists

4 Safety and efficacy

4.1 What are the adverse effects of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Theoretical adverse events

Failed recanalization, cerebral haemorrhage, arterial dissection, recurrent ischaemic stroke, death

2. Anecdotal adverse events (known from experience)

3. Adverse events reported in the literature (if possible please cite literature)

As above

4.2 What are the key efficacy outcomes for this procedure?

Revascularisation achieved with a TICI grade 2b or 3 in > 60% of patients
Rankin Scale 0-2 at 3 months in > 33% of patients
Symptomatic intracranial haemorrhage using SITS definition
Early Death within 72 hours

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

Patient selection
Timing of intervention
Neuro-imaging required
Intervention devices (new vs old)
Cost effectiveness
Deployment of such a service nationally (re-organisation of stroke service to thrombectomy services)
Operator type (neuro-interventional vs other (cardiology/vascular interventionalist)
Effect of age
Basilar artery occlusion (effectiveness)
Tandem lesions
General vs Local anaesthesia
Percentage of stroke population likely to benefit

4.4 What training and facilities are required to undertake this procedure safely?

All doctors must adhere to GMC guidance
Currently procedure is carried out exclusively by consultant interventional neuroradiologists. Individual operators must maintain necessary skills within Neuroscience Department. Regular audit should be undertaken for clinical governance purposes assessing process and outcome of such intervention nationally (SSNAP).

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

Registries include SITS TBY and SSNAP

Major trials that require reporting (THRACE) Not formally published yet.

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, e.g. PUBMED? (This can include your own work). If yes, please list.

THRACE (presented at European stroke organisation, april 2015)

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

There is a strong evidence base that this procedure is effective. The issue is how the intervention will be deployed nationally and by which specialists.

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

5.1 Outcome measures of benefit (including commonly used clinical outcomes – both short and long-term; and quality of life measures):

Lysis to groin puncture < 90 mins
Puncture to start of revascularisation < 45 mins in at least 65 %
Puncture time to end of revascularisation: median < 60 mins
Revascularisation achieved with a TICI grade 2b or 3 in > 60% of patients
Rankin Scale 0-2 at 3 months in > 33% of patients

5.2 Adverse outcomes (including potential early and late complications):

Symptomatic intracranial haemorrhage using SITS definition < 12 %
Early Death within 72 hours

6 Trajectory of the procedure

6.1 In your opinion, what is the likely speed of diffusion of this procedure?

There is a an urgent need to deploy this intervention to the stroke population. Evidence suggest that NNT to treat to achieve a good outcome is between 3-7. There is a requirement to ascertain how effectively this intervention can be delivered within a networked structure either involving designated thrombectomy services under the aegis of Neuroscience or other potential providers that are already in place (cardiology or vascular interventionalists)

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☐ Most or all district general hospitals.

X☐ A minority of hospitals, but at least 10 in the UK.

☐ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

There will probably be a requirement of at least 40 designated specialist neuroscience centres to deliver this intervention.

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

☐ Major.

X☐ Moderate.

☐ Minor.

Comments:

Probably between 5-10% of the stroke population but in particularly patients with the most severe stroke who have the most to gain.

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

8 Data protection and conflicts of interest

8.1 Data protection statement

The Institute is committed to transparency. As part of this commitment your name and specialist society will be placed in the public domain, in future publications and on our website (www.nice.org.uk) and therefore viewable worldwide. This information may be passed to third parties connected with the work on interventional procedures.

A copy of the completed Specialist Adviser advice will be sent to the Specialist Society who nominated the Specialist Adviser.

Specialist Advisers should be aware that full implementation of the Freedom of Information Act 2000 may oblige us to release Specialist Advice from 2005. The Freedom of Information Act 2000 favours the disclosure of information however requests will be considered on a case by case basis. If information is made available, personal information will be removed in accordance with the Data Protection Act 1998. In light of this please ensure that you have not named or identified individuals in your comments.

8.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

Please state any potential conflicts of interest, or any involvements in disputes or complaints, relevant to this procedure. Please use the "Conflicts of Interest for Specialist Advisers" policy (attached) as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

Do you or a member of your family[1] have a **personal pecuniary** interest? The main examples are as follows:

[1] 'Family members' refers to a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible, and adults for whom the member or employee is legally responsible (for example, an adult whose full power of attorney is held by the individual).

Consultancies or directorships attracting regular or occasional payments in cash or kind	☐	**YES**
	☐	**XNO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	☐	**YES**
	☐	**XNO**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☐	**YES**
	☐	**XNO**
Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	☐	**YES**
	☐	**XNO**
Investments – any funds which include investments in the healthcare industry	☐	**YES**
	☐	**XNO**
Do you have a **personal non-pecuniary** interest – eg have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	☐	**YES**
	☐	**XNO**

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry	☐	**YES**
	☐	**XNO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	☐	**YES**
	☐	**XNO**

If you have answered YES to any of the above statements please describe the nature of the conflict(s) below.

Comments:

NO CONFLICT OF INTEREST

Thank you very much for your help.

Professor Bruce Campbell, Chairman, Interventional Procedures Advisory Committee

Professor Carole Longson, Director, Centre for Health Technology Evaluation.

February 2010

Conflicts of Interest for Specialist Advisers

1 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

1.1 Any conflicts of interest set out below should be declared on the questionnaire the Specialist Adviser completes for the procedure.

1.2 Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

2 Personal pecuniary interests

2.1 A personal pecuniary interest involves a current personal payment to a Specialist Adviser, which may either relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as **'specific'** or to the industry or sector from which the product or service comes, in which case it is regarded as **'non-specific'**. The main examples are as follows.

2.1.1 **Consultancies** – any consultancy, directorship, position in or work for the healthcare industry that attracts regular or occasional payments in cash or kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.2 **Fee-paid work** – any work commissioned by the healthcare industry for which the member is paid in cash or in kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.3 **Shareholdings** – any shareholding, or other beneficial interest, in shares of the healthcare industry that are either held by the individual or for which the individual has legal responsibility (for example, children, or relatives whose full Power of Attorney is held by the individual). This does not include shareholdings through unit trusts, pensions funds, or other similar arrangements where the member has no influence on financial management.

2.1.4 **Expenses and hospitality** – any expenses provided by a healthcare industry company beyond that reasonably required for accommodation, meals and travel to attend meetings and conferences (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place.

2.1.5 **Investments** – any funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

2.2 No personal interest exists in the case of:

2.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where

the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

2.2.2 accrued pension rights from earlier employment in the healthcare industry.

3 Personal family interest

3.1 This relates to the personal interests of a family member and involves a **current payment** to the family member of the Specialist Adviser. The interest may relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as '**specific**', or to the industry or sector from which the product or service comes, in which case it is regarded as '**non-specific**'. The main examples include the following.

3.1.1 Any consultancy, directorship, position in or work for a healthcare industry that attracts regular or occasional payments in cash or in kind.

3.1.2 Any fee-paid work commissioned by a healthcare industry for which the member is paid in cash or in kind.

3.1.3 Any shareholdings, or other beneficial interests, in a healthcare industry which are either held by the family member or for which an individual covered by this Code has legal responsibility (for example, children, or adults whose full Power of Attorney is held by the individual).

3.1.4 Expenses and hospitality provided by a healthcare industry company (except where they are provided to a general class of people such as attendees at an open conference)

3.1.5 Funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

3.2 No personal family interest exists in the case of:

3.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

3.2.2 accrued pension rights from earlier employment in the healthcare industry.

4 Personal non-pecuniary interests

These might include, but are not limited to:

4.1 a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review

4.2 a public statement in which an individual covered by this Code has expressed a clear opinion about the matter under consideration, which could reasonably be interpreted as prejudicial to an objective interpretation of the evidence

4.3 holding office in a professional organisation or advocacy group with a direct interest in the matter under consideration

4.4 other reputational risks in relation to an intervention under review.

5 Non-personal interests

5.1 A non-personal interest involves payment that benefits a department or organisation for which a Specialist Advisor is responsible, but that is not received by the Specialist Advisor personally. This may either relate to the product or service being evaluated, in which case it is regarded as **'specific,'** or to the manufacturer or owner of the product or service, but is unrelated to the matter under consideration, in which case it is regarded as **'non-specific'**. The main examples are as follows.

5.1.1 **Fellowships** – the holding of a fellowship endowed by the healthcare industry.

5.1.2 **Support by the healthcare industry or NICE** – any payment, or other support by the healthcare industry or by NICE that does not convey any pecuniary or material benefit to a member personally but that does benefit his/her position or department. For example:

- a grant from a company for the running of a unit or department for which a Specialist Advisor is responsible
- a grant, fellowship or other payment to sponsor a post or member of staff in the unit for which a Specialist Adviser is responsible. This does not include financial assistance for students
- the commissioning of research or other work by, or advice from, staff who work in a unit for which the specialist advisor is responsible
- one or more contracts with, or grants from, NICE.

5.2 Specialist Advisers are under no obligation to seek out knowledge of work done for, or on behalf of, the healthcare industry within departments for which they are responsible if they would not normally expect to be informed.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Procedure Name:	**Mechanical clot retrieval for treating acute ischaemic stroke (1026/2)**
Name of Specialist Advisor:	**Andy Molyneux**
Specialist Society:	**British Society of Neuroradiologists**
Please complete and return to:	azeem.madari@nice.org.uk OR sally.compton@nice.org.uk

1 Do you have adequate knowledge of this procedure to provide advice?

☒ Yes.

☐ No – please return the form/answer no more questions.

1.1 Does the title used above describe the procedure adequately?

☒ Yes.

☐ No. If no, please enter any other titles below.

Comments:

It would be appropriate to adjust the wording of the procedure to " Acute ischaemic stroke due blockage of a major cerebral artery"

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

☒ Yes.

☐ Is there any kind of inter-specialty controversy over the procedure?

☐ No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:

In the UK the procedure is solely done by trained Interventional Neuroradiologists

The next two questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure please answer question 2.2.2.

2.2.1 If you are in a specialty which does this procedure, please indicate your experience with it:

☒ I have never performed this procedure.

☐ I have performed this procedure at least once.

☐ I perform this procedure regularly.

Comments:

I am familiar with the procedure which came into use soon after I ceased doing neuro-interventional cases. I developed the original protocol for the PISTE Trial (Now NIHR funded). I serve on the Data Monitoring Committee of the PISTE Trial.

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☒ I have never taken part in the selection or referral of a patient for this procedure.

☐ I have taken part in patient selection or referred a patient for this procedure at least once.

☐ I take part in patient selection or refer patients for this procedure regularly.

Comments:

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

☐ I have undertaken bibliographic research on this procedure.

☐ I have undertaken research on this procedure in laboratory settings (e.g. device-related research).

☐ I have undertaken clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

☒ Other (please comment) I developed the original protocol for an RCT (PISTE) now funded by NIHR evaluation of Thrombectomy treatment compared with best medical care. As part of my responsibilities on the DMC for the PISTE

trial I am fully familiar with the published and recently presented / reported data from the other RCT's of the procedure. Together with other non-randomised studies of the procedure in the published literature.

Comments:

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

☐ Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter that procedure's safety and efficacy.

☐ Definitely novel and of uncertain safety and efficacy.

☒ The first in a new class of procedure.

Comments:

The recent publication of data from 7 RCT's have shown major clinical benefit compared with standard therapy (thrombolysis) for stroke. See below.

3.2 What would be the comparator (standard practice) to this procedure?

I.V. Thrombolysis for eligible patients and supportive care for those not eligible for thrombolysis.

3.3 Please estimate the proportion of doctors in your specialty who are performing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☒ 10% to 50% of specialists engaged in this area of work.

☐ Fewer than 10% of specialists engaged in this area of work.

☒ Cannot give an estimate.

Comments:

4 Safety and efficacy

4.1 What are the adverse effects of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Theoretical adverse events

Death, symptomatic intracranial haemorrhage, subarachnoid haemorrhage. Vessel rupture. Worsened stroke. Asymptomatic intracranial haemorrhage

Groin haemorrhage, retroperitoneal haemorrhage, secondary to vascular access.

2. Anecdotal adverse events (known from experience)

Death, symptomatic intracranial haemorrhage, subarachnoid haemorrhage. Vessel rupture. Worsened stroke. Asymptomatic intracranial haemorrhage

Groin haemorrhage, retroperitoneal haemorrhage, secondary to vascular access.

3. Adverse events reported in the literature (if possible please cite literature)

Death, symptomatic intracranial haemorrhage, subarachnoid haemorrhage. Vessel rupture. Worsened stroke. Asymptomatic intracranial haemorrhage

Groin haemorrhage, retroperitoneal haemorrhage, secondary to vascular access.

4.2 What are the key efficacy outcomes for this procedure?

90 day clinical outcome based on death and dependency: Modified Rankin scale. Usually done with Rankin shift method.

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

The recent RCT data from 7 separate trials published or presented show major efficacy and clinical outcome improvement over standard medical care for eligible patients.

4.4 What training and facilities are required to undertake this procedure safely?

The procedure requires considerable training in Neurovascular intervention. It is currently limited to interventional Neuroradiologist in the UK,

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

PISTE Trial in the U.K. recruitment suspended at present because of loss of equipoise in the light of the recent trial publications. Consideration is being to re-start based on a modified protocol.

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, e.g. PUBMED? (This can include your own work). If yes, please list.

Recent RCT's published:
(90 day death dependency & Absolute benefit of thrombectomy compared with medical care; AB.)
ESCAPE (Canada & N. Ireland) n = 315: 53% vs 29.3% AB = 23.7%.

SWIFT PRIME trial (Solitaire™ With the Intention For Thrombectomy as PRIMry treatment for acute ischemic strokE) **n= 196 60.2 % vs 35.5%. AB 24.7%.**

Extend – IA: n = 70 pts. 71% vs 40%: AB 31%

MR CLEAN (Holland) n = c400: 32.6% vs 19% AB 13.5%

Recent studies presented at European Stroke Organisation congress in Glasgow.
REVASCAT was presented at ESOC in April and simultaneously published in NEJM. It was conducted over 2 years in just 4 centres in Catalonia, and there was an ongoing registry of all thrombectomy cases in that region: only 8 cases were treated out with the trial, so it closely represents clinical practice.
N = 206 patients, thrombectomy offered improved mRS, aOR 1.7 (95% CI 1.05 – 2.8**)** Symptomatic intracranial haemorrhage was 1.9% in each group
Mortality was 18.4% (thrombectomy) v 15.5% (p=0.6).
increased the proportion with mRS 0-2 at 90 days: 43.7% v 28.2%, aOR 2.1 (95% CI 1.1 – 4.0). **AB 15.5%**

THERAPY was presented at ESOC in April.
It was halted due to loss of equipoise based on external data. Patients received thrombectomy with the PENUMBRA device on top of iv rtPA v rtPA alone.
N = 108 patients in safety evaluation but fewer on efficacy.
Mortality was 12% (thrombectomy) versus 23.9% (thrombolysis), p=0.18.
Primary outcome was 41.5% v 29.3%, p=0.36 and ordinal outcome OR 2.28 (95%1.05 – 4.96), p=0.04. **Absolute Benefit = 12.2%.**
The results are supportive of the other trials, based on under 20% of the planned sample.

THRACE was presented at ESOC French trial a few patients have still to complete follow up**. n = 385:** Thrombectomy on top of iv rtPA as standard care: age 62y, median NIHSS 18,

190 v 195 patients treated at a mean of 4.2h.
Primary outcome (mRS 0-2) was 54.2% v 42.1%, p=0.016; mortality was 12.5% v 13.1%. Adverse events were 27.4% v 30.3%. **Absolute benefit = 15.5%.**

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

The procedure works for patients with major cerebral vessel occlusion who reach hospital in time for treatment (< 4.5 hrs.) and where the facilities and personnel are available. The introduction of a service will require a major re-design of acute stroke services, which may not be possible in some parts of the country, because of logistical, transport and medical and nursing personnel issues.

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

5.1 Outcome measures of benefit (including commonly used clinical outcomes – both short and long-term; and quality of life measures):

30 day and 90 day death and dependency rates.
Symptomatic intracranial haemorrhage rate

5.2 Adverse outcomes (including potential early and late complications):

Death and intracranial and subarachnoid haemorrhage

6 Trajectory of the procedure

6.1 In your opinion, what is the likely speed of diffusion of this procedure?

Very rapid uptake in Neuroscience centres with available INR's elsewhere will need major reorganisation of stroke care, if patients are to benefit.

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☐ Most or all district general hospitals.

☒ A minority of hospitals, but at least 10 in the UK.

☐ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

☒ Major.

☐ Moderate.

☐ Minor.

Comments:

The implications for NHS in England are huge. Both in delivering what is now a proven therapy and the ability to organise and find sufficient experienced medical and nursing support staff to deliver a service,.

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

This is the most important breakthrough in stroke care that has ever been made in my career of more than 30 years involved in the field.
The cost benefit in reducing the number of severely dependent patients after ischaemic stroke is likely to save substantial NHS and Social care resources if this treatment is properly introduced.

8 Data protection and conflicts of interest

8.1 Data protection statement

The Institute is committed to transparency. As part of this commitment your name and specialist society will be placed in the public domain, in future publications and on our website (www.nice.org.uk) and therefore viewable worldwide. This information may be passed to third parties connected with the work on interventional procedures.

A copy of the completed Specialist Adviser advice will be sent to the Specialist Society who nominated the Specialist Adviser.

Specialist Advisers should be aware that full implementation of the Freedom of Information Act 2000 may oblige us to release Specialist Advice from 2005. The Freedom of Information Act 2000 favours the disclosure of information however requests will be considered on a case by case basis. If information is made available, personal information will be removed in accordance with the Data Protection Act 1998. In light of this please ensure that you have not named or identified individuals in your comments.

8.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

Please state any potential conflicts of interest, or any involvements in disputes or complaints, relevant to this procedure. Please use the "Conflicts of Interest for Specialist Advisers" policy (attached) as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

Do you or a member of your family[1] have a **personal pecuniary** interest? The main examples are as follows:

[1] 'Family members' refers to a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible, and adults for whom the member or employee is legally responsible (for example, an adult whose full power of attorney is held by the individual).

Consultancies or directorships attracting regular or occasional payments in cash or kind	☒	**YES**
	☐	**NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	☐	**YES**
	☒	**NO**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☐	**YES**
	☒	**NO**
Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	☐	**YES**
	☒	**NO**
Investments – any funds which include investments in the healthcare industry	☐	**YES**
	☒	**NO**
Do you have a **personal non-pecuniary** interest – eg have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	☐	**YES**
	☒	**NO**

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry	☐	**YES**
	☒	**NO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	☐	**YES**
	☒	**NO**

If you have answered YES to any of the above statements please describe the nature of the conflict(s) below.

Comments:

I am a Consultant to Sequent Medical Inc. providing regulatory and study design advice, and adverse event assessment in respect of A.E's in a clinical trial of an aneurysm treatment device.
I do not have any financial interests or consultancies with in any Stent –retriever technology companies.

I provide paid medical expert witness evidence in cases of stroke and other areas for both NHSLA, defence Societies and Claimant Solicitors.

Thank you very much for your help.

Professor Bruce Campbell, Chairman, Interventional Procedures Advisory

Professor Carole Longson, Director, Centre for Health Technology

Committee	**Evaluation.**
February 2010	

Conflicts of Interest for Specialist Advisers

1 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

1.1 Any conflicts of interest set out below should be declared on the questionnaire the Specialist Adviser completes for the procedure.

1.2 Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

2 Personal pecuniary interests

2.1 A personal pecuniary interest involves a current personal payment to a Specialist Adviser, which may either relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as **'specific'** or to the industry or sector from which the product or service comes, in which case it is regarded as **'non-specific'**. The main examples are as follows.

2.1.1 **Consultancies** – any consultancy, directorship, position in or work for the healthcare industry that attracts regular or occasional payments in cash or kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.2 **Fee-paid work** – any work commissioned by the healthcare industry for which the member is paid in cash or in kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.3 **Shareholdings** – any shareholding, or other beneficial interest, in shares of the healthcare industry that are either held by the individual or for which the individual has legal responsibility (for example, children, or relatives whose full Power of Attorney is held by the individual). This does not include shareholdings through unit trusts, pensions funds, or other similar arrangements where the member has no influence on financial management.

2.1.4 **Expenses and hospitality** – any expenses provided by a healthcare industry company beyond that reasonably required for accommodation, meals and travel to attend meetings and conferences (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place.

2.1.5 **Investments** – any funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

2.2 No personal interest exists in the case of:

2.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where

the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

2.2.2 accrued pension rights from earlier employment in the healthcare industry.

3 Personal family interest

3.1 This relates to the personal interests of a family member and involves a **current payment** to the family member of the Specialist Adviser. The interest may relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as '**specific**', or to the industry or sector from which the product or service comes, in which case it is regarded as '**non-specific**'. The main examples include the following.

3.1.1 Any consultancy, directorship, position in or work for a healthcare industry that attracts regular or occasional payments in cash or in kind.

3.1.2 Any fee-paid work commissioned by a healthcare industry for which the member is paid in cash or in kind.

3.1.3 Any shareholdings, or other beneficial interests, in a healthcare industry which are either held by the family member or for which an individual covered by this Code has legal responsibility (for example, children, or adults whose full Power of Attorney is held by the individual).

3.1.4 Expenses and hospitality provided by a healthcare industry company (except where they are provided to a general class of people such as attendees at an open conference)

3.1.5 Funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

3.2 No personal family interest exists in the case of:

3.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

3.2.2 accrued pension rights from earlier employment in the healthcare industry.

4 Personal non-pecuniary interests

These might include, but are not limited to:

4.1 a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review

4.2 a public statement in which an individual covered by this Code has expressed a clear opinion about the matter under consideration, which could reasonably be interpreted as prejudicial to an objective interpretation of the evidence

4.3 holding office in a professional organisation or advocacy group with a direct interest in the matter under consideration

4.4 other reputational risks in relation to an intervention under review.

5 Non-personal interests

5.1 A non-personal interest involves payment that benefits a department or organisation for which a Specialist Advisor is responsible, but that is not received by the Specialist Advisor personally. This may either relate to the product or service being evaluated, in which case it is regarded as **'specific,'** or to the manufacturer or owner of the product or service, but is unrelated to the matter under consideration, in which case it is regarded as **'non-specific'**. The main examples are as follows.

5.1.1 **Fellowships** – the holding of a fellowship endowed by the healthcare industry.

5.1.2 **Support by the healthcare industry or NICE** – any payment, or other support by the healthcare industry or by NICE that does not convey any pecuniary or material benefit to a member personally but that does benefit his/her position or department. For example:

- a grant from a company for the running of a unit or department for which a Specialist Advisor is responsible
- a grant, fellowship or other payment to sponsor a post or member of staff in the unit for which a Specialist Adviser is responsible. This does not include financial assistance for students
- the commissioning of research or other work by, or advice from, staff who work in a unit for which the specialist advisor is responsible
- one or more contracts with, or grants from, NICE.

5.2 Specialist Advisers are under no obligation to seek out knowledge of work done for, or on behalf of, the healthcare industry within departments for which they are responsible if they would not normally expect to be informed.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Procedure Name:	**Mechanical clot retrieval for treating acute ischaemic stroke (1026/2)**
Name of Specialist Advisor:	**Gerardine Quaghebeur**
Specialist Society:	**British Society of Neuroradiologists**
Please complete and return to:	azeem.madari@nice.org.uk OR sally.compton@nice.org.uk

1 Do you have adequate knowledge of this procedure to provide advice?

X☐ Yes.

☐ No – please return the form/answer no more questions.

1.1 Does the title used above describe the procedure adequately?

X☐ Yes.

☐ No. If no, please enter any other titles below.

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

X☐ Yes.

X☐ Is there any kind of inter-specialty controversy over the procedure?

☐ No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:

there is now no disagreement regarding the efficacy of the procedure in the correct patient population following the publication of at least six trials in the last few months. The controversy relates to which group of "clinicians/radiologists" should be performing the

procedure. The BSNR is of the opinion that only trained interventional neuroradiologists should be performing this procedure; other groups that have expressed an interest within the United Kingdom include cardiologists and in Europe and America these procedures are also performed by neurologists, neuro surgeons and interventional radiologists.

The next two questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure please answer question 2.2.2.

2.2.1 If you are in a specialty which does this procedure, please indicate your experience with it:

X☐ I have never performed this procedure. (I am a diagnostic Neuroradiologist, I have observed colleagues performing the procedure)

☐ I have performed this procedure at least once.

☐ I perform this procedure regularly.

Comments:

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☐ I have never taken part in the selection or referral of a patient for this procedure.

☐ I have taken part in patient selection or referred a patient for this procedure at least once.

☐ I take part in patient selection or refer patients for this procedure regularly.

Comments:

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

X☐ I have undertaken bibliographic research on this procedure.

☐ I have undertaken research on this procedure in laboratory settings (e.g. device-related research).

☐ I have undertaken clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

☐ Other (please comment)

Comments:

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

X☐ Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter that procedure's safety and efficacy.

☐ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

3.2 What would be the comparator (standard practice) to this procedure?

The current standard practice would be intravenous thrombolysis only in those centres where mechanical thrombectomy is not available; in the centres where mechanical thrombectomy is available then standard practice would be intravenous thrombolysis followed by mechanical thrombectomy in appropriately selected patient group

3.3 Please estimate the proportion of doctors in your specialty who are performing this procedure (choose one):

X☐ More than 50% of specialists engaged in this area of work.(interventional neuroradiologists)

☐ 10% to 50% of specialists engaged in this area of work.

☐ Fewer than 10% of specialists engaged in this area of work.

☐ Cannot give an estimate.

Comments:

4 Safety and efficacy

4.1 What are the adverse effects of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Theoretical adverse events

symptomatic intracranial haemorrhage (approximately 5%)

emboli to new vascular territories (approximately 2%)

dissection of the artery (approximately 2%)

vasospasm of the artery being used to access the clot (approximately 3%)

local complications related to arterial puncture (groin haematoma)

2. Anecdotal adverse events (known from experience)

3. Adverse events reported in the literature (if possible please cite literature)

very similar to those listed above

- Neuroradiology. 2014 Jun;56(6):467-76. doi: 10.1007/s00234-014-1352-0. Epub 2014 Mar 26.

  Complications of mechanical thrombectomy for acute ischemic stroke-a retrospective single-center study of 176 consecutive cases.

  Behme D1, Gondecki L, Fiethen S, Kowoll A, Mpotsaris A, Weber W.

4.2 What are the key efficacy outcomes for this procedure?

improved functional outcome assessed by the modified Rankin score at 90 days
essentially improved quality of life for the patient
reduced costs to the NHS as a result of less disablement as a result of acute ischaemic stroke

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

Not to my knowledge

4.4 What training and facilities are required to undertake this procedure safely?

The procedure should only take place in a neuroscience Centre that has a hyper-acute stroke unit within it. There should be access to neurology, neurosurgery and neuro critical care.
There should be an established pathway for intravenous thrombolysis
There should be 24 access to experienced consultant stroke physicians, daily ward rounds, established acute stroke protocols and guidelines, appropriately trained nurses and para-clinical staff.
There needs to be immediate access to brain imaging preferably by means of CT including CT angiography, MRI may be useful in selected cases.
There needs to be 24/7 access to high-quality CT scanning and CTA (CT angiography of the brain and neck vessels) will need to be delivered at the time of the initial CT brain scan. This will require investment of suitable high quality CT scanners in both district general hospitals and tertiary referral centres. This will require recruitment and particularly retention of suitably trained radiographers capable of carrying out these examinations. There will then need to be a system of image exchange whereby the investigation can be reviewed and interpreted by a suitably trained preferably neuroradiologist, at the tertiary centre.
There may need to be training both of neuroradiologists and other clinicians in established in evaluating the CTA examination.
In the tertiary/treatment centre there should be rapid access to a suitable angiography room; neuroscience units should have access to 2 angiography rooms so that there is not competition between stroke and other urgent neuroradiological procedures.
There should be a clear established SOP (standard operating policy) in place with clear indications of time and availability of service provision.
The interventional neuroradiologists (or other groups performing the procedure) must be experienced in utilising intra-arterial devices including mechanical from back to be devices as part of their routine neuro interventional procedures. Most neuro interventionists will have used these devices as part of salvage procedures. It would be appropriate for neuro interventionists to gain further experience or observe intra-arterial therapy in other centres.
There should be adequate number of neuro interventional radiologists available to perform the procedure
there should be adequate number of neuro anaesthetists available to provide whatever the choice of anaesthesia is, conscious sedation appears to be the preferred option.
In my opinion the biggest hurdle will be access to rapid diagnostic CT and CTA; probably as a result of lack of diagnostic radiographers.

4.5 **Are there any major trials or registries of this procedure currently in progress? If so, please list.** I think that most of the major trials are now in print, these are listed below:

- A randomised trial of intra-arterial treatment for acute ischaemic stroke. NEJM 2015; 372:11 to 20, January 1, 2015 Berkhemer et al MR CLEAN
- pooled analysis of IMS III and MR CLEAN trials for patients with NIHSS greater equal to 20. Broderick et al 2015 International stroke conference

- endovascular therapy for ischaemic stroke with perfusion imaging selection. NEJM 2015. Campbell et al
- randomised assessment of rapid endovascular treatment of ischaemic stroke NEJM 2015 Goyal et al
- primary results: swift prime trial NEJM 2015 Saver et al

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, e.g. PUBMED? (This can include your own work). If yes, please list.

No

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

I think the only uncertainty is whether the underlying diagnostic support for initial investigation and CTA will be available; there are also insufficient neuro interventional consultants to provide 24 seven cover, networks may need to be established.

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

5.1 Outcome measures of benefit (including commonly used clinical outcomes – both short and long-term; and quality of life measures):

- revascularisation achieved
- Rankin 0-2 at three months (should be achieved more than 30% of cases)
- symptomatic intracranial haemorrhage using SITS definition, no more than 12% rate should be expected
- early deaths
- audit should include the key process components of any agreed stroke pathway

5.2 Adverse outcomes (including potential early and late complications):

- Early deaths

6 Trajectory of the procedure

6.1 In your opinion, what is the likely speed of diffusion of this procedure?

Rapid

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☐ Most or all district general hospitals.

☐ A minority of hospitals, but at least 10 in the UK.

☐ Fewer than 10 specialist centres in the UK.

X☐ Cannot predict at present.

Comments: as above I think this procedure needs to take place in a specialist neuroscience Centre, and should this occur in all current neuroradiology centres. The provision may require the establishment of networks between centres or local arrangements between different imaging/non-imaging specialists. It is therefore difficult to predict the number of hospitals that will be involved for treatment. All district general hospitals will be required to produce the basic CT and CT angiography upon which a decision can be made, unless all acute stroke patients are admitted directly to a tertiary referral centre

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

X Major.

Moderate.

Minor.

Comments:

The total number of treatments may only come out as a minor to moderate effect or impact on the NHS but the requirement for all patients to be investigated rapidly and assessed for suitability will put major stress onto the diagnostic aspect required to support this service.

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

8 Data protection and conflicts of interest

8.1 Data protection statement

The Institute is committed to transparency. As part of this commitment your name and specialist society will be placed in the public domain, in future publications and on our website (www.nice.org.uk) and therefore viewable worldwide. This information may be passed to third parties connected with the work on interventional procedures.

A copy of the completed Specialist Adviser advice will be sent to the Specialist Society who nominated the Specialist Adviser.

Specialist Advisers should be aware that full implementation of the Freedom of Information Act 2000 may oblige us to release Specialist Advice from 2005. The Freedom of Information Act 2000 favours the disclosure of information however requests will be considered on a case by case basis. If information is made available, personal information will be removed in accordance with the Data Protection Act 1998. In light of this please ensure that you have not named or identified individuals in your comments.

8.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

Please state any potential conflicts of interest, or any involvements in disputes or complaints, relevant to this procedure. Please use the "Conflicts of Interest for Specialist Advisers" policy (attached) as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

Do you or a member of your family[1] have a **personal pecuniary** interest? The main examples are as follows:

[1] 'Family members' refers to a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible, and adults for whom the member or employee is legally responsible (for example, an adult whose full power of attorney is held by the individual).

Consultancies or directorships attracting regular or occasional payments in cash or kind	☐	**YES**
	x ☐	**NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	☐	**YES**
	x ☐	**NO**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☐	**YES**
	x ☐	**NO**
Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	☐	**YES**
	x ☐	**NO**
Investments – any funds which include investments in the healthcare industry	☐	**YES**
	x ☐	**NO**
Do you have a **personal non-pecuniary** interest – eg have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	x ☐	**YES**
	☐	**NO**

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry	☐	**YES**
	x ☐	**NO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	☐	**YES**
	x ☐	**NO**

If you have answered YES to any of the above statements please describe the nature of the conflict(s) below.

Comments:

I Chair the Standards Sub Committee for the BSNR (not sure if relevant?)

Thank you very much for your help.

Professor Bruce Campbell, Chairman, Interventional Procedures Advisory

Professor Carole Longson, Director, Centre for Health Technology Evaluation.

Committee

February 2010

Conflicts of Interest for Specialist Advisers

1 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

1.1 Any conflicts of interest set out below should be declared on the questionnaire the Specialist Adviser completes for the procedure.

1.2 Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

2 Personal pecuniary interests

2.1 A personal pecuniary interest involves a current personal payment to a Specialist Adviser, which may either relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as **'specific'** or to the industry or sector from which the product or service comes, in which case it is regarded as **'non-specific'**. The main examples are as follows.

2.1.1 **Consultancies** – any consultancy, directorship, position in or work for the healthcare industry that attracts regular or occasional payments in cash or kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.2 **Fee-paid work** – any work commissioned by the healthcare industry for which the member is paid in cash or in kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.3 **Shareholdings** – any shareholding, or other beneficial interest, in shares of the healthcare industry that are either held by the individual or for which the individual has legal responsibility (for example, children, or relatives whose full Power of Attorney is held by the individual). This does not include shareholdings through unit trusts, pensions funds, or other similar arrangements where the member has no influence on financial management.

2.1.4 **Expenses and hospitality** – any expenses provided by a healthcare industry company beyond that reasonably required for accommodation, meals and travel to attend meetings and conferences (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place.

2.1.5 **Investments** – any funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

2.2 No personal interest exists in the case of:

2.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where

the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

2.2.2 accrued pension rights from earlier employment in the healthcare industry.

3 Personal family interest

3.1 This relates to the personal interests of a family member and involves a **current payment** to the family member of the Specialist Adviser. The interest may relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as '**specific**', or to the industry or sector from which the product or service comes, in which case it is regarded as '**non-specific**'. The main examples include the following.

3.1.1 Any consultancy, directorship, position in or work for a healthcare industry that attracts regular or occasional payments in cash or in kind.

3.1.2 Any fee-paid work commissioned by a healthcare industry for which the member is paid in cash or in kind.

3.1.3 Any shareholdings, or other beneficial interests, in a healthcare industry which are either held by the family member or for which an individual covered by this Code has legal responsibility (for example, children, or adults whose full Power of Attorney is held by the individual).

3.1.4 Expenses and hospitality provided by a healthcare industry company (except where they are provided to a general class of people such as attendees at an open conference)

3.1.5 Funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

3.2 No personal family interest exists in the case of:

3.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

3.2.2 accrued pension rights from earlier employment in the healthcare industry.

4 Personal non-pecuniary interests

These might include, but are not limited to:

4.1 a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review

4.2 a public statement in which an individual covered by this Code has expressed a clear opinion about the matter under consideration, which could reasonably be interpreted as prejudicial to an objective interpretation of the evidence

4.3 holding office in a professional organisation or advocacy group with a direct interest in the matter under consideration

4.4 other reputational risks in relation to an intervention under review.

5 Non-personal interests

5.1 A non-personal interest involves payment that benefits a department or organisation for which a Specialist Advisor is responsible, but that is not received by the Specialist Advisor personally. This may either relate to the product or service being evaluated, in which case it is regarded as **'specific,'** or to the manufacturer or owner of the product or service, but is unrelated to the matter under consideration, in which case it is regarded as **'non-specific'**. The main examples are as follows.

5.1.1 **Fellowships** – the holding of a fellowship endowed by the healthcare industry.

5.1.2 **Support by the healthcare industry or NICE** – any payment, or other support by the healthcare industry or by NICE that does not convey any pecuniary or material benefit to a member personally but that does benefit his/her position or department. For example:

- a grant from a company for the running of a unit or department for which a Specialist Advisor is responsible
- a grant, fellowship or other payment to sponsor a post or member of staff in the unit for which a Specialist Adviser is responsible. This does not include financial assistance for students
- the commissioning of research or other work by, or advice from, staff who work in a unit for which the specialist advisor is responsible
- one or more contracts with, or grants from, NICE.

5.2 Specialist Advisers are under no obligation to seek out knowledge of work done for, or on behalf of, the healthcare industry within departments for which they are responsible if they would not normally expect to be informed.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Procedure Name:	**Mechanical clot retrieval for treating acute ischaemic stroke (1026/2)**
Name of Specialist Advisor:	**Professor Keith Muir**
Specialist Society:	**British Association of Stroke Physicians (BASP)**
Please complete and return to:	azeem.madari@nice.org.uk OR sally.compton@nice.org.uk

1 Do you have adequate knowledge of this procedure to provide advice?

☒ Yes.

☐ No – please return the form/answer no more questions.

1.1 Does the title used above describe the procedure adequately?

☒ Yes.

☐ No. If no, please enter any other titles below.

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

☒ Yes.

☐ Is there any kind of inter-specialty controversy over the procedure?

☐ No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:

Not yet clear whether there is any controversy between specialties in that all studies have involved only one specialty (interventional neuroradiology), but shortage of this group means

that potential discussion about widening to general interventional radiology, cardiology, or neurology has been raised as an issue.

The next two questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure please answer question 2.2.2.

2.2.1 If you are in a specialty which does this procedure, please indicate your experience with it:

☒ I have never performed this procedure.

☐ I have performed this procedure at least once.

☐ I perform this procedure regularly.

Comments:

Although I have requested it many times and have assisted at procedures on occasion.

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☐ I have never taken part in the selection or referral of a patient for this procedure.

☒ I have taken part in patient selection or referred a patient for this procedure at least once.

☐ I take part in patient selection or refer patients for this procedure regularly.

Comments:

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

☒ I have undertaken bibliographic research on this procedure.

☐ I have undertaken research on this procedure in laboratory settings (e.g. device-related research).

☒ I have undertaken clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

☐ Other (please comment)

Comments:

Currently Chief Investigator of the PISTE trial on this topic.

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

☐ Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter that procedure's safety and efficacy.

☒ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

The statement is not quite correct in that data support efficacy and safety, but only in highly selected patients, and generalisability is uncertain.

3.2 What would be the comparator (standard practice) to this procedure?

Almost all trial patients received intravenous thrombolysis, so this is the relevant comparator.

3.3 Please estimate the proportion of doctors in your specialty who are performing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

☒ Fewer than 10% of specialists engaged in this area of work.

☐ Cannot give an estimate.

Comments:

4 Safety and efficacy

4.1 What are the adverse effects of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Theoretical adverse events

2. Anecdotal adverse events (known from experience)

3. Adverse events reported in the literature (if possible please cite literature)

Embolism to new arterial territory (MR CLEAN trial). Local groin haematoma.

4.2 What are the key efficacy outcomes for this procedure?

Day 90 functional independence assessed by modified Rankin Scale.

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

Generalisability: it is clearly efficacious in selected patients, but what characterises an appropriate patient is less clear.

4.4 What training and facilities are required to undertake this procedure safely?

Interventional neuroradiology team and cath lab; appropriate diagnostic imaging selection (minimum is CT brain and CT angiography, appropriately interpreted to a clear standard, potentially also structured assessment of collateral flow and brain perfusion, which were used in the majority of trials); acute stroke unit environment for patient care before and after.

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

Almost all trials have stopped due to loss of equipoise (including PISTE at present). Only RESILIENT (Brazil) and BASICS (Netherlands, but posterior circulation stroke only) are continuing to recruit to my knowledge.
SITS is running a registry for IA procedures.

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, e.g. PUBMED? (This can include your own work). If yes, please list.

THERAPY and THRACE trials presented at European Stroke Organisation conference but not yet published. Several subgroup or secondary analyses of all trials presented at various international meetings have not yet been published, and several secondary analysis papers not yet published but in stages of submission. Combined individual patient data meta-analysis (TREAT) is planned and protocol for this accepted for publication. European Stroke Organisation guidelines to be updated. American Stroke Association updated guideline statement published in advance online recently (Stroke). PISTE will undertake analysis of initial phase data in the near future but numbers are not large enough to significantly modify the main findings.

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

Case selection unclear; who does the procedure; optimal service organisation; minimum standards for diagnostic imaging for case selection; use of local versus general anaesthesia; generalisability from stent retrievers (almost all of the trial data relate to these devices) to other clot retrieval systems (eg Penumbra) which have minimal data.

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

5.1 Outcome measures of benefit (including commonly used clinical outcomes – both short and long-term; and quality of life measures):

Distribution of Modified Rankin Scale scores day 90
mTICI 2b/3 reperfusion at end of procedure

5.2 Adverse outcomes (including potential early and late complications):

Mortality
New incident stroke rate peri-procedurally (short term)
Proportion referred for hemicraniectomy (short term)

6 Trajectory of the procedure

6.1 In your opinion, what is the likely speed of diffusion of this procedure?

Rapid uptake in specialist centres, immediate demand for access to services from regional stroke centres that exceeds capacity, risk of adopting patient selection criteria that differ substantially from clinical trials and allowing operators not represented in clinical trials (eg cardiologists) to provide the intervention.

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☐ Most or all district general hospitals.

☒ A minority of hospitals, but at least 10 in the UK.

☐ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

But most DGHs will be expected to select appropriate patients for rapid transfer to specialist hubs.

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

☒ Major.

☐ Moderate.

☐ Minor.

Comments:

But equally the benefits may be very large since this applies only to a group of patients for whom current best treatment leaves a high proportion dead or significantly disabled. The resource use therefore likely represents a shift of resource from long-term care to acute settings.

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

8 Data protection and conflicts of interest

8.1 Data protection statement

The Institute is committed to transparency. As part of this commitment your name and specialist society will be placed in the public domain, in future publications and on our website (www.nice.org.uk) and therefore viewable worldwide. This information may be passed to third parties connected with the work on interventional procedures.

A copy of the completed Specialist Adviser advice will be sent to the Specialist Society who nominated the Specialist Adviser.

Specialist Advisers should be aware that full implementation of the Freedom of Information Act 2000 may oblige us to release Specialist Advice from 2005. The Freedom of Information Act 2000 favours the disclosure of information however requests will be considered on a case by case basis. If information is made available, personal information will be removed in accordance with the Data Protection Act 1998. In light of this please ensure that you have not named or identified individuals in your comments.

8.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

Please state any potential conflicts of interest, or any involvements in disputes or complaints, relevant to this procedure. Please use the "Conflicts of Interest for Specialist Advisers" policy (attached) as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

Do you or a member of your family[1] have a **personal pecuniary** interest? The main examples are as follows:

[1] 'Family members' refers to a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible, and adults for whom the member or employee is legally responsible (for example, an adult whose full power of attorney is held by the individual).

Consultancies or directorships attracting regular or occasional payments in cash or kind	☐	**YES**
	☒	**NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	☐	**YES**
	☒	**NO**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☐	**YES**
	☒	**NO**
Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	☐	**YES**
	☒	**NO**
Investments – any funds which include investments in the healthcare industry	☐	**YES**
	☒	**NO**
Do you have a **personal non-pecuniary** interest – eg have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	☐	**YES**
	☒	**NO**

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry	☐	**YES**
	☒	**NO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	☒	**YES**
	☐	**NO**

If you have answered YES to any of the above statements please describe the nature of the conflict(s) below.

Comments:

The University of Glasgow received support in terms of non-specific grants from Codman and Covidien to support patient recruitment, and trial running in the first phase of the PISTE Trial. The main funding for the first phase of PISTE was provided by the Stroke Association; and for the main phase of the trial by the NIHR Health Technology Assessment programme. I am Chief Investigator and grant holder for these awards.

Thank you very much for your help.

Professor Bruce Campbell, Chairman, Interventional Procedures Advisory Committee

Professor Carole Longson, Director, Centre for Health Technology Evaluation.

February 2010

Conflicts of Interest for Specialist Advisers

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2.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where

the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

2.2.2 accrued pension rights from earlier employment in the healthcare industry.

3 Personal family interest

3.1 This relates to the personal interests of a family member and involves a **current payment** to the family member of the Specialist Adviser. The interest may relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as '**specific**', or to the industry or sector from which the product or service comes, in which case it is regarded as '**non-specific**'. The main examples include the following.

3.1.1 Any consultancy, directorship, position in or work for a healthcare industry that attracts regular or occasional payments in cash or in kind.

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3.2.2 accrued pension rights from earlier employment in the healthcare industry.

4 Personal non-pecuniary interests

These might include, but are not limited to:

4.1 a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review

4.2 a public statement in which an individual covered by this Code has expressed a clear opinion about the matter under consideration, which could reasonably be interpreted as prejudicial to an objective interpretation of the evidence

4.3 holding office in a professional organisation or advocacy group with a direct interest in the matter under consideration

4.4 other reputational risks in relation to an intervention under review.

5 Non-personal interests

5.1 A non-personal interest involves payment that benefits a department or organisation for which a Specialist Advisor is responsible, but that is not received by the Specialist Advisor personally. This may either relate to the product or service being evaluated, in which case it is regarded as **'specific,'** or to the manufacturer or owner of the product or service, but is unrelated to the matter under consideration, in which case it is regarded as **'non-specific'**. The main examples are as follows.

5.1.1 **Fellowships** – the holding of a fellowship endowed by the healthcare industry.

5.1.2 **Support by the healthcare industry or NICE** – any payment, or other support by the healthcare industry or by NICE that does not convey any pecuniary or material benefit to a member personally but that does benefit his/her position or department. For example:

- a grant from a company for the running of a unit or department for which a Specialist Advisor is responsible
- a grant, fellowship or other payment to sponsor a post or member of staff in the unit for which a Specialist Adviser is responsible. This does not include financial assistance for students
- the commissioning of research or other work by, or advice from, staff who work in a unit for which the specialist advisor is responsible
- one or more contracts with, or grants from, NICE.

5.2 Specialist Advisers are under no obligation to seek out knowledge of work done for, or on behalf of, the healthcare industry within departments for which they are responsible if they would not normally expect to be informed.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Procedure Name:	**Mechanical clot retrieval for treating acute ischaemic stroke (1026/2)**
Name of Specialist Advisor:	**Phil White**
Specialist Society:	**British Society of Neuroradiologists**
Please complete and return to:	azeem.madari@nice.org.uk OR sally.compton@nice.org.uk

1 Do you have adequate knowledge of this procedure to provide advice?

X Yes.

☐ No – please return the form/answer no more questions.

1.1 Does the title used above describe the procedure adequately?

X Yes.

☐ No. If no, please enter any other titles below.

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

X Yes.

X Is there any kind of inter-specialty controversy over the procedure?

☐ No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:

All the evidence to date on mechanical clot retrieval safety/efficacy is from cases undertaken in trials by trained experienced Neurointerventional practitioners – in the UK all of these are interventional neuroradiologists (INRs). A small reduction in

technical success and/or a small increase in procedure related complications could obviate ALL/most of the clinical benefit of the procedure.

Other professional groups who undertake vascular procedures elsewhere in the body have published that they should do it too. However, there are major issues over training & skill maintenance for intracranial thrombectomy in non INRs in the UK at present – so this aspect is controversial.

The next two questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure please answer question 2.2.2.

2.2.1 If you are in a specialty which does this procedure, please indicate your experience with it:

☐ I have never performed this procedure.

☐ I have performed this procedure at least once.

X I perform this procedure regularly.

Comments:

Experience = >24 in total with >14 in last 3y. My unit has randomised more patients into thrombectomy trials than other in UK – 22 to date

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☐ I have never taken part in the selection or referral of a patient for this procedure.

☐ I have taken part in patient selection or referred a patient for this procedure at least once.

X I take part in patient selection or refer patients for this procedure regularly.

Comments:

European/Canadian/Australian patients comprise the bulk of randomised patients in the published/presented trials (on imaging selection based thrombectomy) to date. Overwhelmingly in Europe/Canada/Australia the procedure is performed by INRs.

MR CLEAN/THRACE/REVASCAT/EXTEND IA all from these countries & a high proportion of SWIFT PRIME & ESCAPE patients are also from Europe/Canada.

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

X I have undertaken bibliographic research on this procedure.

☐ I have undertaken research on this procedure in laboratory settings (e.g. device-related research).

X I have undertaken clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

X Other (please comment)

Comments:

I am also involved as co-lead in developing a health economics model for thrombectomy (HTA funded) project as part of the HTA PEARS [Promoting Rapid And Effective Stroke care] programme grant

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

☐ Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter that procedure's safety and efficacy.

☐ Definitely novel and of uncertain safety and efficacy.

X The first in a new class of procedure.

Comments:

But thrombectomy has very recently proven safe & highly effective in multiple RCTs when undertaken by trained experienced Neurointerventional practitioners with appropriate neuroimaging based patient selection

3.2 What would be the comparator (standard practice) to this procedure?

IV thrombolysis alone or in some cases no active therapy

3.3 Please estimate the proportion of doctors in your specialty who are performing this procedure (choose one):

X More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

☐ Fewer than 10% of specialists engaged in this area of work.

☐ Cannot give an estimate.

Comments:

Almost all UK units with INR capability have performed this procedure within the last 2y (data from UKNG & PEARS surveys)

4 Safety and efficacy

4.1 What are the adverse effects of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Theoretical adverse events

2. Anecdotal adverse events (known from experience)

3. Adverse events reported in the literature (if possible please cite literature)

- Death (1-2% procedure related but 10-20% overall in thrombectomy arms of trials)
- Intracerebral haemorrhage (SICH 0-10% in trials)
- Subarachnoid Haemorrhage (5-15%)
- anaphylaxis to contrast or IV thrombolytic
- groin puncture site complications (haematoma, infection, pseudoaneurysm),
- infections, PE, other stroke related

- see 5 recent RCT papers in NEJM for fuller bibliography

RCTs: NEJM Dec 2014 MR CLEAN

2015 – ESCAPE/EXTEND IA (Feb); SWIFT PRIME & REVASCAT trials (April)

ESO presentations April 2015 – TRHACE & THEARPY trials

UK PISTE trial- analysis of start-up phase in process. Recruitment stopped in May.

4.2 What are the key efficacy outcomes for this procedure?

- Clinical status as 90 days as assessed by validated scales including modified Rankin Score (mRS), Oxford Handicap Score, Barthel Index
- Quality of life measures – including validated scores for depression after stroke, EUROQuol etc
- Technical success in terms of vascular recanalisation as assessed by validated scale such as modified TICI [Thrombolysis in cerebral infarction] scale
- Timeline metrics of procedure (time form stroke onset to diagnosis of LVO then time from diagnosis to groin puncture then time from puncture to final recanalisation achieved)

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

Advanced brain imaging and its' interpretation are critical to patient triage & selection and thus the overall efficacy of thrombecotmy – as witnessed by the considerable variation in benefit in trials – ranging from 8% in THERAPY to 31% in EXTEND IA (% refer to absolute difference [benefit for thrombectomy] in mRS 0-2 at 90 days)!

There are major uncertainties over the optimum imaging and triage approach – CT/CTA with thrombectomy in all positive for large vessel occlusion or a more imaging refined selection using CT Perfusion or equivalent.
Head to head trials do not exist (yet) & answering this by comparing trials is difficult/impossible as there are major population demographic & timelines differences and country/health economy differences between them

4.4 What training and facilities are required to undertake this procedure safely?

- Accredited/credentialed training in neuroendovascular interventional procedures – in the UK the only recognised programme is via obtaining CCT in Radiology(IR) where the training follows the RCR developed (& GMC approved) curriculum for interventional radiology (IR) including neurointervention

- Accredited training in neuroimaging to be able to correctly/accurately interpret complex brain imaging in a very time pressured clinical situation – including brain perfusion imaging, non-invasive cerebral angiography, MRI brain. In the UK the only recognised programme is via obtaining CCT in Radiology

- Regularly undertaking cerebral intracranial interventional procedures is essential to maintain skills – minimum of 40 cerebral vascular interventional cases per annum was suggested in an earlier multidisciplinary consensus statement [Society of British Neurological Surgeons and Brit Soc. Neuroradiologists]. This cerebral vascular interventional workload should now include regular stroke thrombectomy

- Biplane neuroangiography suite is optimum equipment with anaesthetic support in angio room, immediate availability of neurocritical care, immediate availability of neurosurgery (for ICH/hydrocephalus/craniectomy & other complication management)

- Familiarity with & experience in a) neuroimaging and b) equipment required to deal with complications – including coils/liquid embolics/retrieval devices as well as multiple devices used for thrombectomy

- Excellent links between stroke team & endovascular team including regular (weekly) radiology multidisciplinary conference involving both teams

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

As above THRACE/THERAPY trials presented but yet to publish

- Extended or unknown time onset trials – DAWN, THRILL, & a POSITIVE trial ongoing
- Posterior circulation – BASICS 2 trial ongoing
- Proposed PISTE 2 – will be a head to head trial of IAT+IVT for all LVO versus IVT+ imaging selection for IAT - using CT Perfusion to identify cases suitable for IAT and with detailed cost effectiveness ascertainment built in

Major registries – German National Registry & multinational SITS-Thrombectomy

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, e.g. PUBMED? (This can include your own work). If yes, please list.

THRACE/THERAPY
PISTE – I am co CI for this trial and this is in the process of analysis of completed start-up phase – 65 patients all randomised in England

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

<u>Important uncertainty</u>

- Whether to triage using advanced brain imaging (fewer patients have IAT but benefit greater in trials) or whether to do IAT in all large vessel occlusive (LVO) strokes? – this question has massive implications for NHS service redesign & delivery
- Whether timelines for thrombectomy can be extended beyond 6h
- Whether works in posterior circulation (only proven in anterior cerebral circulation)
- Whether thrombectomy should be done in more distal cerebral vessels – M2, ACA, P2 etc.
- Whether thrombectomy works in strokes of unknown time onset with appropriate imaging selection
- Which imaging approach is best – CTP or MRI or collateral scoring
- True cost effectiveness

<u>Controversy</u>

- Should IAT be the sole treatment? – is IVT useful/necessary in LVO stroke if expeditious IAT can be performed – no trial yet but may come soon
- Who should do it- only trained experienced Neurointerventional practitioners (RCT data based on this) or extend to any endovascular practitioner
- If extend to practiotners beyond evidence base is this within a collaboration with experienced neurointerventionists (for training/support/mentoring) or “standalone”

It may be helpful to explain that in the UK (as in most of Western Europe) all cerebral neuroendovascular procedures (including thrombectomy for stroke) within the NHS are undertaken within neuroscience centres by INRs under specialised commissioning arrangements for neuroscience.
No other professional group in the UK has existing training/experience in cerebral endovascular interventions. GMC guidance is clear that operators should not normally carry out procedures with which they are unfamiliar

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

Adherence to clinical pathway - % not managed/imaged within pathway
Safety – key metrics: death within 72h, SICH, other ICH, procedural Cx rates
Efficacy

- Clinical outcome at 90/7 by mRS
- Prcoedural TIC 2b/3 rates

Time metrics

- Onset to diagnosis of LVO stroke
- Diagnosis of LVO to groin puncture
- Groin puncture to final recanalisation

Health Ecomomcs metrics

- Hospital admission duration & ITU/Critical care component
- Procedure consumable cost
- Days at home by 90/7

5.1 Outcome measures of benefit (including commonly used clinical outcomes – both short and long-term; and quality of life measures):

As listed earlier

5.2 Adverse outcomes (including potential early and late complications):

As listed earlier

6 Trajectory of the procedure

6.1 In your opinion, what is the likely speed of diffusion of this procedure?

Rapid increase in activity within stroke centres that have access on site to INRs or IRs who can be supported closely by INRs.

- The predicted numbers depend upon the imaging triage approach adopted.
- If all confirmed acute LVO strokes are referred for thrombectomy the number may exceed 200 per million population per annum & then increase further as the RCT evidence base for thrombectomy extends
- However if a more selective imaging approach is used to identify those who are unlikely to benefit is adopted (as EXTEND IA trial) then the numbers are more likely to be in range 50-80 per million per annum increasing somewhat as proven indications extend

In centres without INR service it is currently uncertain whether they will pursue collaboration with local regional neurosciences services (hub and spoke as for cancer/cardiology) or whether some will seek to develop ad hoc local provision by non-experts. Here the lack of expert neuroimaging support locally will be just as critical an obstacle to **safe** provision as lack of expert neuroendovascular expertise

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☐ Most or all district general hospitals.

X A minority of hospitals, but at least 10 in the UK.

☐ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

As above.
The procedure has been undertaken in at least 26 of the 28 UK units with neuroscience centres that possess INR capability within the last 2 years

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

X Major.

☐ Moderate.

☐ Minor.

Comments:

Stroke service redesign is inevitable but how significant it will need to be remains unclear in my view due to the multiple & important uncertainties highlighted above where more research is required/outcome awaited if ongoing

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

8 Data protection and conflicts of interest

8.1 Data protection statement

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	☐	**NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	☐	**YES**
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Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☐	**YES**
	X	**NO**
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		NO

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry	**X**	**YES**
	☐	**NO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	**X**	**YES**
	☐	**NO**

If you have answered YES to any of the above statements please describe the nature of the conflict(s) below.

Comments:

Personal non-pecuniary: I am the elected secretary of UK Neurointerventional Group and this is a professional medical organisation with a direct interest in the topic. I am also a member of the British Soc. Neuroradiologists standards committee – another professional medical organisation with a direct interest in the topic. I represent the Royal College of Radiologists on the intercollegiate stroke working party, which clearly has a direct interest in the topic. I also sit on the Stroke Association charity research grant awards committee

Non-personal: I co-hold research grants part funded by industry for PISTE & STABILISE thrombectomy trials administered via University of Glasgow and Newcastle University respectively. One of these grants supports a 3y clinical PhD post in Newcastle.

Personal pecuniary: I undertake occasional consultancy work for healthcare industry including manufacturers of devices used for stroke thrombectomy, which is all medical professional teaching/education activity – course/conferences supported by industry – 4 in the last 2 years which have occurred (3) / planned (1)

Thank you very much for your help.

Professor Bruce Campbell, Chairman, Interventional Procedures Advisory Committee

Professor Carole Longson, Director, Centre for Health Technology Evaluation.

February 2010

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the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

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3.1.4 Expenses and hospitality provided by a healthcare industry company (except where they are provided to a general class of people such as attendees at an open conference)

3.1.5 Funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

3.2 No personal family interest exists in the case of:

3.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

3.2.2 accrued pension rights from earlier employment in the healthcare industry.

4 Personal non-pecuniary interests

These might include, but are not limited to:

4.1 a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review

4.2 a public statement in which an individual covered by this Code has expressed a clear opinion about the matter under consideration, which could reasonably be interpreted as prejudicial to an objective interpretation of the evidence

4.3 holding office in a professional organisation or advocacy group with a direct interest in the matter under consideration

4.4 other reputational risks in relation to an intervention under review.

5 Non-personal interests

5.1 A non-personal interest involves payment that benefits a department or organisation for which a Specialist Advisor is responsible, but that is not received by the Specialist Advisor personally. This may either relate to the product or service being evaluated, in which case it is regarded as **'specific,'** or to the manufacturer or owner of the product or service, but is unrelated to the matter under consideration, in which case it is regarded as **'non-specific'**. The main examples are as follows.

5.1.1 **Fellowships** – the holding of a fellowship endowed by the healthcare industry.

5.1.2 **Support by the healthcare industry or NICE** – any payment, or other support by the healthcare industry or by NICE that does not convey any pecuniary or material benefit to a member personally but that does benefit his/her position or department. For example:

- a grant from a company for the running of a unit or department for which a Specialist Advisor is responsible
- a grant, fellowship or other payment to sponsor a post or member of staff in the unit for which a Specialist Adviser is responsible. This does not include financial assistance for students
- the commissioning of research or other work by, or advice from, staff who work in a unit for which the specialist advisor is responsible
- one or more contracts with, or grants from, NICE.

5.2 Specialist Advisers are under no obligation to seek out knowledge of work done for, or on behalf of, the healthcare industry within departments for which they are responsible if they would not normally expect to be informed.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Procedure Name:	**Mechanical clot retrieval for treating acute ischaemic stroke (1026/2)**
Name of Specialist Advisor:	**Professor Pippa Tyrrell**
Specialist Society:	**British Association of Stroke Physicians (BASP)**
Please complete and return to:	azeem.madari@nice.org.uk OR sally.compton@nice.org.uk

1 Do you have adequate knowledge of this procedure to provide advice?

X☐ Yes.

☐ No – please return the form/answer no more questions.

1.1 Does the title used above describe the procedure adequately?

X☐ Yes.

☐ No. If no, please enter any other titles below.

Comments:

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

X☐ Yes.

☐ Is there any kind of inter-specialty controversy over the procedure?

☐ No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:

There is excellent RCT evidence now to support the use of this technology in selected patients in acute stroke. The challenge will be implementation of the evidence.

The next two questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure please answer question 2.2.2.

2.2.1 If you are in a specialty which does this procedure, please indicate your experience with it:

X☐ I have never performed this procedure.

☐ I have performed this procedure at least once.

☐ I perform this procedure regularly.

Comments:

This procedure is performed by neuroradiologists

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☐ I have never taken part in the selection or referral of a patient for this procedure.

X☐ I have taken part in patient selection or referred a patient for this procedure at least once.

☐ I take part in patient selection or refer patients for this procedure regularly.

Comments:

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

☐x I have undertaken bibliographic research on this procedure.

☐ I have undertaken research on this procedure in laboratory settings (e.g. device-related research).

☐ I have undertaken clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

☐ Other (please comment)

Comments: I have been involved in the review of evidence for the ICSWP guideline and I have commented on the research for the Stroke association

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

☐ Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter that procedure's safety and efficacy.

☐ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

I do not think that I can tick any of the above boxes. It is a practice that has been performed for some years, in small numbers. The evidence has taken time to accumulate but is now there.

3.2 What would be the comparator (standard practice) to this procedure?

iv thrombolysis (but it is likely that many patients will receive iv thrombolysis and then proceed to thrombectomy "drip and ship")

3.3 Please estimate the proportion of doctors in your specialty who are performing this procedure (choose one):

☐ More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

☐ Fewer than 10% of specialists engaged in this area of work.

☒ Cannot give an estimate.

Comments:

It is Neuroradiologists who perform this and not stroke physicians. It is very important that they take part in this work

4 Safety and efficacy

4.1 What are the adverse effects of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Theoretical adverse events

Arterial rupture, intracerebral bleeding, problems with the catheter, local bleeding

2. Anecdotal adverse events (known from experience)

As above

3. Adverse events reported in the literature (if possible please cite literature)

As above http://europepmc.org/abstract/MED/26002302

http://europepmc.org/abstract/MED/24401478

http://europepmc.org/abstract/MED/25944326

http://europepmc.org/abstract/MED/26159790

this is just a small selection; massive literature when you search!

4.2 What are the key efficacy outcomes for this procedure?

Mortality and 3 month modified rankin score

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

No, see literature

4.4 What training and facilities are required to undertake this procedure safely?

Interventional Neuroradiologists do this procedure
Training for stroke clinicians in who to refer and how
Training for stroke nurses and HDU nurses in after care
Neuroanaesthesia support

Paramedic training for transfer of pts between centres for drip and ship

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

Yes, easily availbale in the literature

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, e.g. PUBMED? (This can include your own work). If yes, please list.

Yes, lots when you search including a Karolinska review at the end of 2014

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

No, it is the implementation that is the big challenge

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

5.1 Outcome measures of benefit (including commonly used clinical outcomes – both short and long-term; and quality of life measures):

mortality
Symptomatic secondary ICH
6 month mRS

5.2 Adverse outcomes (including potential early and late complications):

Death and disability
sICH

6 Trajectory of the procedure

6.1 In your opinion, what is the likely speed of diffusion of this procedure?

Depends on our ability to implement

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☐ Most or all district general hospitals.

X☐ A minority of hospitals, but at least 10 in the UK.

☐ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

Ideally one per region

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

☐ Major.

X☐ Moderate.

☐ Minor.

Comments:

Probably relatively small numbers of patients but huge implications for service delivery

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

8 Data protection and conflicts of interest

8.1 Data protection statement

The Institute is committed to transparency. As part of this commitment your name and specialist society will be placed in the public domain, in future publications and on our website (www.nice.org.uk) and therefore viewable worldwide. This information may be passed to third parties connected with the work on interventional procedures.

A copy of the completed Specialist Adviser advice will be sent to the Specialist Society who nominated the Specialist Adviser.

Specialist Advisers should be aware that full implementation of the Freedom of Information Act 2000 may oblige us to release Specialist Advice from 2005. The Freedom of Information Act 2000 favours the disclosure of information however requests will be considered on a case by case basis. If information is made available, personal information will be removed in accordance with the Data Protection Act 1998. In light of this please ensure that you have not named or identified individuals in your comments.

8.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

Please state any potential conflicts of interest, or any involvements in disputes or complaints, relevant to this procedure. Please use the "Conflicts of Interest for Specialist Advisers" policy (attached) as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

Do you or a member of your family[1] have a **personal pecuniary** interest? The main examples are as follows:

[1] 'Family members' refers to a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible, and adults for whom the member or employee is legally responsible (for example, an adult whose full power of attorney is held by the individual).

Consultancies or directorships attracting regular or occasional payments in cash or kind	☐	**YES**
	x ☐	**NO**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	☐	**YES**
	x ☐	**NO**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	☐	**YES**
	x ☐	**NO**
Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	☐	**YES**
	x ☐	**NO**
Investments – any funds which include investments in the healthcare industry	☐	**YES**
	☐	**NO**
Do you have a **personal non-pecuniary** interest – eg have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	x	**YES**
	☐	**NO**

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry	☐	**YES**
	☐	**NO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	☐	**YES**
	☐	**NO**

If you have answered YES to any of the above statements please describe the nature of the conflict(s) below.

Comments:
I am medical Vice Chair of the Stroke association and I know they will want to make independent comments on the topic and are organising a meeting which I will attend. I am associate director RCP stroke programme and involved in writing ICSWP guidelines.

Thank you very much for your help.

Professor Bruce Campbell, Chairman, Interventional Procedures Advisory Committee

Professor Carole Longson, Director, Centre for Health Technology Evaluation.

February 2010

Conflicts of Interest for Specialist Advisers

1 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

1.1 Any conflicts of interest set out below should be declared on the questionnaire the Specialist Adviser completes for the procedure.

1.2 Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

2 Personal pecuniary interests

2.1 A personal pecuniary interest involves a current personal payment to a Specialist Adviser, which may either relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as **'specific'** or to the industry or sector from which the product or service comes, in which case it is regarded as **'non-specific'**. The main examples are as follows.

2.1.1 **Consultancies** – any consultancy, directorship, position in or work for the healthcare industry that attracts regular or occasional payments in cash or kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.2 **Fee-paid work** – any work commissioned by the healthcare industry for which the member is paid in cash or in kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.3 **Shareholdings** – any shareholding, or other beneficial interest, in shares of the healthcare industry that are either held by the individual or for which the individual has legal responsibility (for example, children, or relatives whose full Power of Attorney is held by the individual). This does not include shareholdings through unit trusts, pensions funds, or other similar arrangements where the member has no influence on financial management.

2.1.4 **Expenses and hospitality** – any expenses provided by a healthcare industry company beyond that reasonably required for accommodation, meals and travel to attend meetings and conferences (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place.

2.1.5 **Investments** – any funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

2.2 No personal interest exists in the case of:

2.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where

the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

2.2.2 accrued pension rights from earlier employment in the healthcare industry.

3 Personal family interest

3.1 This relates to the personal interests of a family member and involves a **current payment** to the family member of the Specialist Adviser. The interest may relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as '**specific**', or to the industry or sector from which the product or service comes, in which case it is regarded as '**non-specific**'. The main examples include the following.

3.1.1 Any consultancy, directorship, position in or work for a healthcare industry that attracts regular or occasional payments in cash or in kind.

3.1.2 Any fee-paid work commissioned by a healthcare industry for which the member is paid in cash or in kind.

3.1.3 Any shareholdings, or other beneficial interests, in a healthcare industry which are either held by the family member or for which an individual covered by this Code has legal responsibility (for example, children, or adults whose full Power of Attorney is held by the individual).

3.1.4 Expenses and hospitality provided by a healthcare industry company (except where they are provided to a general class of people such as attendees at an open conference)

3.1.5 Funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

3.2 No personal family interest exists in the case of:

3.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

3.2.2 accrued pension rights from earlier employment in the healthcare industry.

4 Personal non-pecuniary interests

These might include, but are not limited to:

4.1 a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review

4.2 a public statement in which an individual covered by this Code has expressed a clear opinion about the matter under consideration, which could reasonably be interpreted as prejudicial to an objective interpretation of the evidence

4.3 holding office in a professional organisation or advocacy group with a direct interest in the matter under consideration

4.4 other reputational risks in relation to an intervention under review.

5 Non-personal interests

5.1 A non-personal interest involves payment that benefits a department or organisation for which a Specialist Advisor is responsible, but that is not received by the Specialist Advisor personally. This may either relate to the product or service being evaluated, in which case it is regarded as **'specific,'** or to the manufacturer or owner of the product or service, but is unrelated to the matter under consideration, in which case it is regarded as **'non-specific'**. The main examples are as follows.

5.1.1 **Fellowships** – the holding of a fellowship endowed by the healthcare industry.

5.1.2 **Support by the healthcare industry or NICE** – any payment, or other support by the healthcare industry or by NICE that does not convey any pecuniary or material benefit to a member personally but that does benefit his/her position or department. For example:

- a grant from a company for the running of a unit or department for which a Specialist Advisor is responsible
- a grant, fellowship or other payment to sponsor a post or member of staff in the unit for which a Specialist Adviser is responsible. This does not include financial assistance for students
- the commissioning of research or other work by, or advice from, staff who work in a unit for which the specialist advisor is responsible
- one or more contracts with, or grants from, NICE.

5.2 Specialist Advisers are under no obligation to seek out knowledge of work done for, or on behalf of, the healthcare industry within departments for which they are responsible if they would not normally expect to be informed.

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Interventional Procedures Programme

Procedure Name:	**Mechanical clot retrieval for treating acute ischaemic stroke (1026/2)**
Name of Specialist Advisor:	**Tony Goddard**
Specialist Society:	**British Society of Neuroradiologists**
Please complete and return to:	azeem.madari@nice.org.uk OR sally.compton@nice.org.uk

1 Do you have adequate knowledge of this procedure to provide advice?

X Yes.

☐ No – please return the form/answer no more questions.

1.1 Does the title used above describe the procedure adequately?

X Yes.

☐ No. If no, please enter any other titles below.

Comments:

The title encompasses the current variations of the procedure (stent retriever and aspiration thrombectomy, and their various combinations.

2 Your involvement in the procedure

2.1 Is this procedure relevant to your specialty?

X Yes.

X Is there any kind of inter-specialty controversy over the procedure?

☐ No. If no, then answer no more questions, but please give any information you can about who is likely to be doing the procedure.

Comments:

There are issues over who performs the procedure. The BSNR and UKNG feel strongly that it should be interventional neuroradiologists who perform this procedure due to the training and

experience required. However, there is a body of opinion from interventional cardiologists that they have the on call infrastructure to provide the service. In the U.S. interventional neurologists are also providing this service. However, in the UK there does not seem to be an appetite amongst our neurologists to engage in the procedure.

The next two questions are about whether you carry out the procedure, or refer patients for it. If you are in a specialty that normally carries out the procedure please answer question 2.2.1. If you are in a specialty that normally selects or refers patients for the procedure please answer question 2.2.2.

2.2.1 If you are in a specialty which does this procedure, please indicate your experience with it:

☐ I have never performed this procedure.

☐ I have performed this procedure at least once.

x I perform this procedure regularly.

Comments:

I have performed this procedure on over 100 patients.

2.2.2 If your specialty is involved in patient selection or referral to another specialty for this procedure, please indicate your experience with it.

☐ I have never taken part in the selection or referral of a patient for this procedure.

☐ I have taken part in patient selection or referred a patient for this procedure at least once.

x I take part in patient selection or refer patients for this procedure regularly.

Comments:

In general, interventionists are involved in patient selection for this procedure. This is mainly due to the fact that image interpretation is a crucial factor in determining suitability for thrombolysis, along with clinical criteria such as stroke severity and time form onset.

2.3 Please indicate your research experience relating to this procedure (please choose one or more if relevant):

x I have undertaken bibliographic research on this procedure.

x I have undertaken research on this procedure in laboratory settings (e.g. device-related research).

x I have undertaken clinical research on this procedure involving patients or healthy volunteers.

☐ I have had no involvement in research on this procedure.

☐ Other (please comment)

Comments: I have participated in a major clinical trial on this procedure (PISTE).
I have also extensively researched the literature on stroke treatment. I have published several articles on stroke intervention and given national and international lectures on the subject.
I have also been involved in more basic research on efficacy of current technology on thrombus retrieval in the laboratory.

3 Status of the procedure

3.1 Which of the following best describes the procedure (choose one):

x Established practice and no longer new.

☐ A minor variation on an existing procedure, which is unlikely to alter that procedure's safety and efficacy.

☐ Definitely novel and of uncertain safety and efficacy.

☐ The first in a new class of procedure.

Comments:

The procedure (stent retriever) has been available for well over 5 years now in various forms, and before that interventional techniques were first utilised for stroke treatment in the 1980's. It is hardly new. There is now a good level of evidence from randomised controlled trials (at least 6), case series, and personal experience that the procedure is safe.
The issue currently is selecting patients who may benefit, as not all stroke patients do.

3.2 What would be the comparator (standard practice) to this procedure?

In a most patients it would be:

1. Intravenous thrombolysis
2. Standard medical care in those who have a contraindication to thrombolysis

3.3 Please estimate the proportion of doctors in your specialty who are performing this procedure (choose one):

x More than 50% of specialists engaged in this area of work.

☐ 10% to 50% of specialists engaged in this area of work.

☐ Fewer than 10% of specialists engaged in this area of work.

☐ Cannot give an estimate.

Comments:

4 Safety and efficacy

4.1 What are the adverse effects of the procedure?

Please list adverse events and major risks (even if uncommon) and, if possible, estimate their incidence, as follows:

1. Theoretical adverse events
    1. Reperfusion injury
    2. Contrast allergy
    3. Futile recanalization: recanalisation too late to help patient
    4. Device malfunction- degeneration of internal structure
2. Anecdotal adverse events (known from experience)
    1. Stentriever entrapment
    2. Vasospasm
    3. Middle cerebral artery dissection
    4. Embolus to different territory
    5. Distal embolisation beyond site of initial thrombus
3. Adverse events reported in the literature (if possible please cite literature)
    1. Intracerebral haemorrhage
    2. Carotid dissection
    3. Carotid rupture (personal experience)
    4. Groin haematoma
    5. Femoral artery dissection

4.2 What are the key efficacy outcomes for this procedure?

1. Improvement in NIHSS score
2. MRS outcome scores at discharge and follow-up
3. Recanalisation as measured by internationally accepted TICI scores
4. Reduction in mortality
5. Cost-effectiveness. This is important, as stroke survivors require significant care and any intervention that reduces the number of dependent survivors might have a significant impact on treatment costs.

4.3 Are there uncertainties or concerns about the *efficacy* of this procedure? If so, what are they?

Patient selection is key – some come too late and not all do well even with technically successful treatment. This is a universal problem in medicine, though.

4.4 What training and facilities are required to undertake this procedure safely?

These procedures are not always straightforward. Most require skills to navigate complex aortic arch, cervical and intracranial vascular anatomy. Moreover, an understanding of stroke physiology is important in deciding whom to treat. Management of difficulties and complications is vitally important. What to do with carotid stenosis (do you stent and how?), what catheter and stent do you use? What happens if you can't navigate to the occlusion? Most interventions require more than one pass and device. How do you know when to stop?

4.5 Are there any major trials or registries of this procedure currently in progress? If so, please list.

Current trials are as below (www.snisonline.org):

1. ReStore Thrombectomy Trial for Flow Restoration in Acute Ischemic Stroke Patients
Prospective, multicenter, randomized study comparing the safety and efficacy of the ReStore Thrombectomy Device with the MERCI Retrieval System in acute ischemic stroke patients who require mechanical thrombectomy. Study sponsor is Reverse Medical Corporation. Recruitment is currently suspended.

2. Trial and Cost Effectiveness Evaluation of Intra-arterial Thrombectomy in Acute Ischemic Stroke (THRACE)
Randomized, controlled, multicenter trial comparing outcomes and cost effectiveness of a combined approach of IV thrombolysis plus mechanical thrombectomy to the reference treatment of IV thrombolysis alone in patients who present with acute ischemic stroke within four hours of symptom onset. Study sponsor is Central Hospital, Nancy, France. Currently recruiting participants.

3. Pragmatic Ischaemic Stroke Thrombectomy Evaluation (PISTE)

Randomized, controlled trial of adjunctive mechanical thrombectomy (in addition to IV thrombolysis) compared with IV thrombolysis alone in patients with acute ischemic stroke. Study sponsor is NHS Greater Glasgow and Clyde. Study is not yet open for recruitment.

4. Endovascular Treatment for Small Core and Proximal Occlusion Ischemic Stroke (ESCAPE)
Randomized, controlled trial evaluating whether rapid endovascular revascularization amongst radiologically selected (small core/proximal occlusion) patients with ischemic stroke within 12 hours of last seen normal results in improved outcomes compared to patients treated with best standard of medical care, including IV thrombolysis to those eligible. Study sponsor is University of Calgary. Enrolling participants by invitation only.

5. Solitaire FR Thrombectomy for Acute Revascularisation (STAR)
Observational clinical evaluation of the safety and efficacy of the Solitaire FR Device in acute ischemic stroke patients requiring mechanical thrombectomy when used according to its Instructions For Use. Study sponsor is ev3. Study is ongoing but not recruiting patients.

6. Percutaneous Recanalization in Ischemic Stroke Management in Europe Observational Registry (PRIISM2)
Prospective, observational, cohort study to determine the revascularization rate, clinical efficacy, and safety of the CE-marked MindFrame System in ischemic stroke patients. Study sponsor is MindFrame, Inc. The study is ongoing, but not recruiting participants.

7. POSITIVE Stroke Clinical Trial
Randomized trial to determine the safety and efficacy of intra-arterial reperfusion in acute ischemic stroke patients ineligible for IV-TPA as selected by physiologic imaging. Study sponsor is Medical University of South Carolina. This study is not yet open for participant recruitment.

8. Assess the Penumbra System in the Treatment of Acute Stroke (THERAPY)
Randomized, controlled trial to assess the safety and effectiveness of the Penumbra System as an adjunctive treatment to IV-TPA in patients with acute ischemic stroke from large vessel occlusion in the brain. Patients must be eligible to receive IV-TPA and have evidence of a large clot burden (clot length > 8 mm). Study sponsor is Penumbra, Inc. This study is currently recruiting participants.

9. Penumbra Imaging Collaborative Study (PICS)
Observational cohort study whose primary aim is to gather data on the “real world” experience of the Penumbra System and to determine if there is a correlation between the imaging-defined size of the ischemic penumbra at admission and the outcomes in patients already treated by the System. Study sponsor is Penumbra, Inc. This study is ongoing, but not recruiting participants.

10. Solitaire™ FR as Primary Treatment for Acute Ischemic Stroke (SWIFT PRIME)
Randomized, controlled trial to determine if patients with acute ischemic stroke due to a large vessel occlusion treated with combined IV-TPA and Solitaire FR within 6 hours of symptom onset have less stroke-related disability than those patients treated with IV TPA alone. Study sponsor is Covidien. This study is currently recruiting participants.

11. ADAPT: A Direct Aspiration, First Pass Technique for the Endovascular Treatment of Stroke
Retrospective, observational, multicenter study comparing a direct aspiration, first pass technique to traditional thrombectomy devices in patients undergoing thrombectomy for acute stroke. Study sponsor is Medical University of South Carolina. This study is not yet open for participant recruitment.

12. A Randomized, Concurrent Controlled Trial to Assess the Safety and Effectiveness of the Separator 3D as a Component of the Penumbra System in the Revascularization of Large Vessel Occlusion in Acute Ischemic Stroke
Prospective, randomized, controlled, multicenter trial evaluating the safety and effectiveness of the Penumbra Separator 3D as a component of the Penumbra System for the revascularization of large vessel occlusion in acute ischemic stroke. Patients will be assigned to either the Penumbra System with the Separator 3D or

the Penumbra System alone without the Separator 3D. Study sponsor is Penumbra, Inc. This study is currently recruiting participants.

13. Feasibility Study of IV rtPA vs. Primary Endovascular Therapy for Acute Ischemic Stroke (EARLY)
Randomized pilot trial comparing endovascular reperfusion therapy to IV-TPA in patients able to receive the assigned treatment within 4.5 hours of symptom onset. Study sponsor is Mayo Clinic. This study is currently recruiting participants.

14. Extending the Time for Thrombolysis in Emergency Neurological Deficits - Intra-Arterial (EXTEND-IA)
Randomized, controlled trial comparing intra-arterial reperfusion therapy with the Solitaire device after standard dose IV-TPA to IV-TPA alone in patients with acute ischemic stroke. Patients must be eligible to receive IV-TPA within 4.5 hours of symptom onset, and demonstrate a large vessel occlusion and mismatch on imaging. Study sponsor is National Stroke Research Institute, Australia. This study is currently recruiting participants.

15. Swiss Intravenous and Intra-arterial Thrombolysis for Treatment of Acute Ischemic Stroke Registry (SWISS)
Observational cohort study of patients with acute ischemic stroke treated with IV or IA thrombolysis in a Swiss stroke unit. Clinical and radiographical data will be evaluated. Study sponsor is University Hospital Inselspital, Berne. This study is currently recruiting participants.

16. Wake up Symptomatic Stroke - Benefit of Intravenous Clot Busters or Endovascular Intervention (WASSABI)
Randomized trial studying the safety and effectiveness of using CT Perfusion studies as an indicator to treat stroke patients with unknown time of onset. Patients will be assigned to standard medical therapy, IV thrombolysis, or intra-arterial intervention. Study sponsor is Jacobs Neurological Institute. This study is currently recruiting participants.

17. Sedation Versus General Anesthesia for Endovascular Therapy in Acute Stroke - Impact on Neurological Outcome (ANSTROKE)
Prospective, randomized study to evaluate whether general anesthesia or sedation technique is preferable during embolectomy for acute stroke, measured in terms of three month neurological impairment and complication frequency between the methods. Study sponsor is Sahlgrenska University Hospital, Sweden. This study is currently recruiting participants.

18. Endovascular Revascularization With Solitaire Device Versus Best Medical Therapy in Anterior Circulation Stroke Within 8 Hours (REVASCAT)
Prospective, multicenter, randomized, controlled trial to evaluate the hypothesis that mechanical embolectomy with the Solitaire FR device is superior to medical management alone (including IV-TPA) in achieving favorable outcomes in the distribution of mRS scores at 90 days in patients presenting with acute large vessel ischemic stroke < 8 hours from symptom onset. Study sponsor is Fundacio Ictus Malaltia Vascular. This study is currently recruiting participants.

19. Basilar Artery International Cooperation Study (BASICS)
Randomized, controlled, multicenter trial evaluating the efficacy and safety of additional intra-arterial treatment after IV thrombolysis in patients with basilar artery occlusion confirmed by CTA or MRA. Eligible patients must receive IV thrombolysis within 4.5 hours from symptom onset. Patients will be randomized between additional

intra-arterial treatment after IV thrombolysis or IV thrombolysis alone. Study sponsor is Erik van der Hoeven, St. Antonius Hospital. This study is currently recruiting participants.

20. International Multicenter Registry for Mechanical Recanalization Procedures in Acute Stroke (ENDOSTROKE)
Observational cohort study to gather information on predictors of good or poor clinical outcome following mechanical recanalization therapies for acute ischemic stroke. Study sponsor is Goethe University. This study is currently recruiting participants.

21. Computed Tomography Perfusion (CTP) to Predict Response to Recanalization in Ischemic Stroke Project (CRISP)
In the first part of this study, the investigators propose to develop a fully automated CTP analysis program. Part two is a prospective cohort study to demonstrate that this CTP analysis program can help accurately identify acute stroke patients who are likely to benefit from endovascular therapy. Study sponsor is Stanford University. This study is currently recruiting participants.

22. Imaging Guided Patient Selection for Interventional Revascularization Therapy (START)
Non-randomized, single group study to determine the safety and effectiveness of the Penumbra System in a stroke cohort who presents within 8 hours from symptom onset and with a known core infarct volume on admission. The study will also determine if there is a correlation between infarct volume and functional outcome in treated patients at 90 days post-procedure. Study sponsor is Penumbra, Inc. This study is ongoing, but not recruiting participants.

23. Endovascular Acute Stroke Intervention Trial - the EASI Trial
Randomized, controlled multicentric trial, with a parallel comparison between standard and combined (standard plus thrombectomy) treatment. Study sponsor is CHUM Notre-Dame hospital, Montreal, Canada. Currently recruiting participants.

4.6 Are you aware of any abstracts that have been *recently* presented/ published on this procedure that may not be listed in a standard literature search, e.g. PUBMED? (This can include your own work). If yes, please list.

See Pubmed – there are at least 30 abstracts already in 2015 regarding aspects of intra-arterial stroke treatment.

4.7 Is there controversy, or important uncertainty, about any aspect of the way in which this procedure is currently being done or disseminated?

As with all novel techniques, we are still learning which patients will benefit the most from intervention. Imaging is key and neuroradiology experience in interpretation is crucial. Unlike heart attack where there may be ECG and blood enzyme changes, no such definitive criteria exist to even support an initial diagnosis of stroke. Once a likely clinical diagnosis is established, there are a variety of imaging modalities available to confirm this and assess cerebral perfusion and potential suitability for treatment. These are best interpreted by a neuroradiologist.

The safety profile seems established.

Clinical outcome criteria

5 Audit Criteria

Please suggest a minimum dataset of criteria by which this procedure could be audited.

5.1 Outcome measures of benefit (including commonly used clinical outcomes – both short and long-term; and quality of life measures):

1. Reperfusion using Thrombolysis In Cerebral Ischaemia criteria
2. Reduction in NIHSS score pre and post treatment.
3. Modified Rankin Score

5.2 Adverse outcomes (including potential early and late complications):

1. Procedural complications
2. Symptomatic intracranial haemorrhage
3. Failure to improve despite successful treatment (case selection issue)
4. Groin complications: significant haematoma.; femoral artery damage

6 Trajectory of the procedure

6.1 In your opinion, what is the likely speed of diffusion of this procedure?

I suspect it will be limited by the difficulties in service delivery. The majority of UK neuroscience centres are offering this treatment to patients in their own region. However, there are significant limitations in providing a comprehensive service as there are a limited number of trained individuals to provide the treatment.
Another factor is infrastructure required to move patients quickly to where treatment can be offered.
Finally is funding this. Increased numbers if trained specialists, centralisation of services etc etc

6.2 This procedure, if safe and efficacious, is likely to be carried out in (choose one):

☐ Most or all district general hospitals.

X A minority of hospitals, but at least 10 in the UK.

☐ Fewer than 10 specialist centres in the UK.

☐ Cannot predict at present.

Comments:

Specialist personnel and angiographic equipment are required and these are not readily available in all hospitals. It is the concentration of skilled and experienced clinicians that is the most important deciding factor.

6.3 The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, is:

X Major.

☐ Moderate.

☐ Minor.

Comments:

This procedure, in selected patients has shown clinical benefit and is cost-effective. It doubles the number of independent survivors.

7 Other information

7.1 Is there any other information about this procedure that might assist NICE in assessing the possible need to investigate its use?

I have attached a recent editorial from this month's Neurosurgery journal which is a good summary of current status.

8 Data protection and conflicts of interest

8.1 Data protection statement

The Institute is committed to transparency. As part of this commitment your name and specialist society will be placed in the public domain, in future publications and on our website (www.nice.org.uk) and therefore viewable worldwide. This information may be passed to third parties connected with the work on interventional procedures.

A copy of the completed Specialist Adviser advice will be sent to the Specialist Society who nominated the Specialist Adviser.

Specialist Advisers should be aware that full implementation of the Freedom of Information Act 2000 may oblige us to release Specialist Advice from 2005. The Freedom of Information Act 2000 favours the disclosure of information however requests will be considered on a case by case basis. If information is made available, personal information will be removed in accordance with the Data Protection Act 1998. In light of this please ensure that you have not named or identified individuals in your comments.

8.2 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

Please state any potential conflicts of interest, or any involvements in disputes or complaints, relevant to this procedure. Please use the "Conflicts of Interest for Specialist Advisers" policy (attached) as a guide when declaring any conflicts of interest. Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

Do you or a member of your family[1] have a **personal pecuniary** interest? The main examples are as follows:

[1] 'Family members' refers to a spouse or partner living in the same residence as the member or employee, children for whom the member or employee is legally responsible, and adults for

Consultancies or directorships attracting regular or occasional payments in cash or kind	**x**	**YES**
Fee-paid work – any work commissioned by the healthcare industry **– this includes income earned in the course of private practice**	**x**	**YES**
Shareholdings – any shareholding, or other beneficial interest, in shares of the healthcare industry	**x**	**NO**
Expenses and hospitality – any expenses provided by a healthcare industry company beyond those reasonably required for accommodation, meals and travel to attend meetings and conferences	**x**	**YES**
Investments – any funds which include investments in the healthcare industry	**x**	**NO**
Do you have a **personal non-pecuniary** interest – eg have you made a public statement about the topic or do you hold an office in a professional organisation or advocacy group with a direct interest in the topic?	**x**	**NO**

Do you have a **non-personal** interest? The main examples are as follows:

Fellowships endowed by the healthcare industry	**x**	**NO**
Support by the healthcare industry or NICE that benefits his/her position or department, eg grants, sponsorship of posts	**x**	**NO**

If you have answered YES to any of the above statements please describe the nature of the conflict(s) below.

Comments:

Both Codman and Stryker, who both manufacture intra-arterial devices for stroke treatment have financially supported attendance at international meetings. I have also advised Codman on trials relating to stroke treatment in Japan.

Thank you very much for your help.

Professor Bruce Campbell, Chairman, Interventional Procedures Advisory Committee

Professor Carole Longson, Director, Centre for Health Technology Evaluation.

February 2010

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whom the member or employee is legally responsible (for example, an adult whose full power of attorney is held by the individual).

Conflicts of Interest for Specialist Advisers

1 Declarations of interest by Specialist Advisers advising the NICE Interventional Procedures Advisory Committee

1.1 Any conflicts of interest set out below should be declared on the questionnaire the Specialist Adviser completes for the procedure.

1.2 Specialist Advisers should seek advice if required from the Associate Director – Interventional Procedures.

2 Personal pecuniary interests

2.1 A personal pecuniary interest involves a current personal payment to a Specialist Adviser, which may either relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as **'specific'** or to the industry or sector from which the product or service comes, in which case it is regarded as **'non-specific'**. The main examples are as follows.

2.1.1 **Consultancies** – any consultancy, directorship, position in or work for the healthcare industry that attracts regular or occasional payments in cash or kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.2 **Fee-paid work** – any work commissioned by the healthcare industry for which the member is paid in cash or in kind (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place).

2.1.3 **Shareholdings** – any shareholding, or other beneficial interest, in shares of the healthcare industry that are either held by the individual or for which the individual has legal responsibility (for example, children, or relatives whose full Power of Attorney is held by the individual). This does not include shareholdings through unit trusts, pensions funds, or other similar arrangements where the member has no influence on financial management.

2.1.4 **Expenses and hospitality** – any expenses provided by a healthcare industry company beyond that reasonably required for accommodation, meals and travel to attend meetings and conferences (this includes both those which have been undertaken in the 12 months preceding the point at which the declaration is made and which are planned but have not taken place.

2.1.5 **Investments** – any funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

2.2 No personal interest exists in the case of:

2.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where

the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

2.2.2 accrued pension rights from earlier employment in the healthcare industry.

3 Personal family interest

3.1 This relates to the personal interests of a family member and involves a **current payment** to the family member of the Specialist Adviser. The interest may relate to the manufacturer or owner of a product or service being evaluated, in which case it is regarded as '**specific**', or to the industry or sector from which the product or service comes, in which case it is regarded as '**non-specific**'. The main examples include the following.

3.1.1 Any consultancy, directorship, position in or work for a healthcare industry that attracts regular or occasional payments in cash or in kind.

3.1.2 Any fee-paid work commissioned by a healthcare industry for which the member is paid in cash or in kind.

3.1.3 Any shareholdings, or other beneficial interests, in a healthcare industry which are either held by the family member or for which an individual covered by this Code has legal responsibility (for example, children, or adults whose full Power of Attorney is held by the individual).

3.1.4 Expenses and hospitality provided by a healthcare industry company (except where they are provided to a general class of people such as attendees at an open conference)

3.1.5 Funds which include investments in the healthcare industry that are held in a portfolio over which individuals have the ability to instruct the fund manager as to the composition of the fund.

3.2 No personal family interest exists in the case of:

3.2.1 assets over which individuals have no financial control (for example, wide portfolio unit trusts and occupational pension funds) and where the fund manager has full discretion as to its composition (for example, the Universities Superannuation Scheme)

3.2.2 accrued pension rights from earlier employment in the healthcare industry.

4 Personal non-pecuniary interests

These might include, but are not limited to:

4.1 a clear opinion, reached as the conclusion of a research project, about the clinical and/or cost effectiveness of an intervention under review

4.2 a public statement in which an individual covered by this Code has expressed a clear opinion about the matter under consideration, which could reasonably be interpreted as prejudicial to an objective interpretation of the evidence

4.3 holding office in a professional organisation or advocacy group with a direct interest in the matter under consideration

4.4 other reputational risks in relation to an intervention under review.

5 Non-personal interests

5.1 A non-personal interest involves payment that benefits a department or organisation for which a Specialist Advisor is responsible, but that is not received by the Specialist Advisor personally. This may either relate to the product or service being evaluated, in which case it is regarded as **'specific,'** or to the manufacturer or owner of the product or service, but is unrelated to the matter under consideration, in which case it is regarded as **'non-specific'**. The main examples are as follows.

5.1.1 **Fellowships** – the holding of a fellowship endowed by the healthcare industry.

5.1.2 **Support by the healthcare industry or NICE** – any payment, or other support by the healthcare industry or by NICE that does not convey any pecuniary or material benefit to a member personally but that does benefit his/her position or department. For example:

- a grant from a company for the running of a unit or department for which a Specialist Advisor is responsible
- a grant, fellowship or other payment to sponsor a post or member of staff in the unit for which a Specialist Adviser is responsible. This does not include financial assistance for students
- the commissioning of research or other work by, or advice from, staff who work in a unit for which the specialist advisor is responsible
- one or more contracts with, or grants from, NICE.

5.2 Specialist Advisers are under no obligation to seek out knowledge of work done for, or on behalf of, the healthcare industry within departments for which they are responsible if they would not normally expect to be informed.