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# A prospective multicentre double blind placebo controlled trial to evaluate the effectiveness of patent foramen ovale (PFO) closure with the STARFlex® septal repair implant to resolve refractory migraine headache

**Submission date**
15/11/2004

**Recruitment status**
No longer recruiting

**Registration date**
09/02/2005

**Overall study status**
Completed

**Last Edited**
07/03/2008

**Condition category**
Nervous System Diseases

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

**Plain English summary of protocol**
Not provided at time of registration

**Study website**
http://www.migraine-mist.org/index.asp

## Contact information

**Type(s)**
Scientific

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## Additional identifiers

**EudraCT/CTIS number**

### IRAS number

### ClinicalTrials.gov number

### Secondary identifying numbers
MIST01

# Study information

### Scientific Title

### Acronym
MIST - Migraine Intervention with STARFlex® Technology

### Study objectives
To investigate the effect of PFO closure with the STARFlex® Septal Repair Implant System in a selected refractory migraine with aura population on the resolution of migraine attacks.

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
MREC approved 04/11/2004

### Study design
A prospective, multicentre, double blind, placebo controlled parallel group trial

### Primary study design
Interventional

### Secondary study design
Randomised controlled trial

### Study setting(s)
Not specified

### Study type(s)
Not Specified

### Participant information sheet

### Health condition(s) or problem(s) studied
PFO/Migraine

### Interventions
Double blinded study randomising migraine patients with PFOs to either PFO closure with the STARFlex® implant or a control arm who received a sham procedure, assessments of PFO were

made using trans oesophageal echo and trans thoracic echo. Baseline headache data has been obtained for both groups and has been followed up with 6 months of post-procedure headache diary data and physicians' assessments of migraine profile for both implant and placebo groups.

## Intervention Type
Other

## Phase
Not Specified

## Primary outcome measure
Incidence of migraine headache during the 90 days analysis period following the healing phase.

## Secondary outcome measures
1. Incidence of migraine during the healing phase (the first 90 days post procedure)
2. Change in the severity of migraine attacks, based on MIDAS (Migraine Disability Assessment) and HIT-6 (Headache Impact Test) scores
3. Change in the frequency of migraine attacks other than elimination of attacks
4. Change in characteristics of migraine (with or without aura and change thereon)
5. Change in severity, frequency and character of migraine relative to effective closure rate or presence of residual leak
6. Change in quality of life based on SF36-v2 QOL survey

The secondary endpoints of safety are:
7. Device success, defined as successful delivery of one or more STARFlex® device(s) to the site during the index procedure without a procedural complication, deployment of the device at the intended site, and removal of the delivery system
8. Procedural success, defined as device success without the occurrence of procedural complications prior to discharge, including device embolisation, cerebral or pulmonary embolism, cardiac perforation, and infective endocarditis

The secondary endpoints of failure are:
9. Incidence of major adverse events from the STARFlex® Septal Repair Implant
10. Incidence of major vascular access complications related to the index procedure, including access site haematoma >5 cm, false aneurysm, AV fistula, retroperitoneal bleed, peripheral ischaemia/nerve injury, procedure related transfusion, and the need for vascular surgical repair or ultrasound compression
11. Incidence of adverse drug reactions to medications used in the index procedure
12. Incidence of adverse drug reactions to procedure specific medications required during the follow phase
13. Major bleeding, defined as the occurrence of intracranial, intraocular, or retroperitoneal hemorrhage or any hemorrhage requiring a blood transfusion during the index hospitalisation, or during the follow-up time period
14. Death (due to any cause) during the first 30 days following treatment
15. Death caused directly by a malfunction of the implant after the first 30 days
16. Incidence of other major adverse events

The tertiary endpoints of efficacy are:
17. Relationship between PFO and associated atrial septal aneurysm and frequency of migraine

18. Relationship between patient sex and change in migraine frequency, or severity
19. Effective closure rate, defined as procedural success with either grade 0 (none) or 1 (trace) residual shunt as measured by TTE at 180210 days post-procedure

### Overall study start date
24/11/2004

### Completion date
31/05/2005

## Eligibility

### Key inclusion criteria
Patients with refractory migraine

Inclusion criteria:
1. The patient is greater than or equal to 18 years of age and less than or equal to 60 years of age
2. Patients must meet the definition of 'with aura'
3. Patients with a history of migraine onset prior to age 50
4. Patients must meet the definition of refractory migraine
5. Patients must have a positive contrast valsalva bubble trial by TTE, demonstrating grade 2 or 3 right to left shunting. An atrial septal aneurysm may or may not be identified.
6. Patients must be available for follow-up in accordance with the protocol
7. The patient is able to provide a signed informed consent form signed at three stages to participate. Informed consent from guardians is not acceptable.
8. Patients critical cardiac structures are not expected to come in contact with the device (e.g. AV valves and pulmonary veins). It is recommended that the device be approximately 1 mm from these structures.
9. Patients must agree not to get pregnant during the trial

Post-randomisation - Device Patients Only:
10. The vascular access from the femoral vein is expected to accommodate the 11F delivery system
11. The size of the PFO (measured by indentation with a soft balloon) must demonstrate the defect to be amenable to selection of a STARFlex® Septal Repair Implant as described in the Instructions for Use

### Participant type(s)
Patient

### Age group
Adult

### Lower age limit
18 Years

### Sex
Both

### Target number of participants

150 - first patient was enrolled 24/11/04, last patient 31/05/05

## Key exclusion criteria

1. Patients are less than 18, or greater than 60, years of age
2. Failure to meet the definition of migraine 'with aura'
3. Failure to meet the definition of refractory migraine
4. A contrast valsalva bubble study demonstrates no or trivial shunting from right to left through a PFO
5. Any cardiovascular condition, including those requiring chronic medications that would interfere with the conduct or assessment of outcome of the trial, or that would increase patient risk relative to undergoing the procedure or with the ability to deliver and deploy the STARFlex® Septal Repair System
6. Inability of the patient to personally give and sign the informed consent
7. A large, redundant atrial septal aneurysm which cannot, in the judgment of the investigator, be covered by the STARFlex® Septal Repair System without (1) causing the device to interfere with other intracardiac structures, or (2) prohibiting the ability of the operator to adequately deploy the distal/proximal arms in the left/right atrium prior to final placement on the septum.
8. Patients with an elongated waist (long tunnel), any other reason requiring Transseptal puncture for device placement
9. Other cardiac defects, whether or not repaired, including: Atrial septal defect; Ventricular septal defect; Coarctation of the aorta; Patent ductus arteriosus; or Mitral or aortic stenosis.
10. Thrombus in or occlusion of the venous lumen between the femoral vein access site (or superior access site, if used) and the right atrium
11. A previously implanted atrial septal device
12. Echocardiography evidence of an intra-atrial or ventricular thrombus
13. History of drug abuse
14. Known active endocarditis or documented bacteraemia
15. Elevated serum creatinine such that the use of contrast dye during the implant procedure would expose the patient to unnecessary risks of additional renal dysfunction
16. Active infections requiring current antibiotic therapy (if temporary illness, patients may enroll after discontinuation of antibiotics, once asymptomatic for 4 weeks)
17. Patients who are pregnant, nursing, or planning pregnancy over the duration of the patients participation in the study
18. A known sensitivity to medications used in general anaesthesia
19. A known contraindication to aspirin or clopidogrel
20. Sensitivity to contrast media, which cannot be adequately pre-medicated
21. A platelet count <100,000 cells/mm3 or >700,000 cells/mm3, or a WBC of <3,000 cells/mm3, or a known disorder of platelet function

22. Any patient with a known coagulopathy for which they are currently being treated medically with anticoagulants
23. Patients with any neurological disorder or disease that would interfere with proper assessment and or conduct of the trial

24. Patients unable to perform a satisfactory valsalva manoeuvre
25. Patients in whom transoesophageal echocardiography is contraindicated
26. Active peptic ulcer or upper gastrointestinal bleeding within the prior 6 months
27. Concurrent medical condition with a life expectancy of less than 12 months
28. Currently participating in an investigational drug or another device trial that has not completed the primary endpoint or that clinically interferes with the current trial endpoints. [NOTE: Trials requiring extended follow-up for products that were investigational, but have since become commercially available, are not considered investigational trials.]

29. The presence of a permanent pacemaker
30. The presence of an inferior vena cava filter
31. Haemodynamic conditions generally contraindicating closure of a PFO or any other right to left decompressive shunt. (i.e., normal RV function and PVR >10 indexed Wood units if RV pressure <1/2 systemic pressure or, PVR >8 indexed Wood units if RV pressure >1/2 systemic pressure)
32. If echocardiography suggests moderate or greater tricuspid regurgitation
33. Suspected/recognised cirrhosis or portal hypertension or known pulmonary arterio-venous malformations
34. Any PFO that requires closure for reasons unrelated to the migraine history (e.g., orthodeoxia, stroke, TIA, decompression illness)
35. Patients known to be headache medication over users
36. Patients diagnosed with chronic daily headache
37. Patients with a documented medical history of oesophageal stricture, diverticulae, symptomatic hiatus hernia, oesophagitis or oesophageal varices
38. If in the investigators opinion, the patient is unsuitable to be entered in the trial for any other reason

### Date of first enrolment
24/11/2004

### Date of final enrolment
31/05/2005

## Locations

### Countries of recruitment
England

United Kingdom

### Study participating centre
**King's Healthcare**
London
United Kingdom
SE5 9RS

## Sponsor information

### Organisation
NMT Medical Inc. (USA)

### Sponsor details

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### Sponsor type
Industry

# Funder(s)

### Funder type
Industry

### Funder Name
NMT Medical Inc. (USA)

# Results and Publications

### Publication and dissemination plan
Not provided at time of registration

### Intention to publish date

### Individual participant data (IPD) sharing plan

### IPD sharing plan summary
Not provided at time of registration

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Results article | Results | 18/03/2008 | | Yes | No |