

# Stretta System for gastro-oesophageal reflux disease

Medtech innovation briefing

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## Summary

- The **technology** described in this briefing is the Stretta System. It applies radiofrequency (RF) energy to the lower oesophageal sphincter and gastric cardia to improve symptoms of gastro-oesophageal reflux disease (GORD).
- The **innovative aspects** are that this is the only RF energy device for treating GORD. Stretta Therapy is minimally invasive and can be done under sedation in an outpatient endoscopy suite, or under general anaesthesia as a day case procedure.
- The **intended place in therapy** would be for treating GORD symptoms, which cannot be controlled using proton pump inhibitor (PPI) medication therapy, alongside surgery, or before surgery. NICE interventional procedures guidance on [endoscopic radiofrequency ablation for gastro-oesophageal reflux disease](#) recommends that, because of uncertainty over longer-term safety and inconclusive efficacy evidence, the procedure should only be used with special arrangements for clinical governance, consent and audit or research.
- The **key points from the evidence** summarised in this briefing come from 5 studies (n=588) published after the interventional procedures guidance was published. The evidence suggests that Stretta Therapy improves symptom scores and reduces PPI medication dependence up to 5 years after treatment when compared with baseline. No additional objective efficacy evidence has been published.

- **Key uncertainties** around the evidence are that none of the published studies were set in the UK. There are no comparative studies of Stretta Therapy against other endoscopic treatments of GORD.
- The Stretta System costs £2,495 for the single-use delivery catheter and £25,000 for the reusable RF generator, excluding VAT.

## The technology

The Stretta System is a radiofrequency (RF) energy device intended to treat gastro-oesophageal reflux disease (GORD). During the procedure, known as Stretta Therapy, RF energy is delivered to treatment sites above and below the gastro-oesophageal junction. The manufacturer states that Stretta Therapy is non-ablative because it does not remove or destroy tissue, but regenerates the target tissue by creating hypertrophy that thickens the musculature to improve GORD symptoms.

The Stretta System consists of a reusable, pole-mounted 4-channel RF generator and a sterile, single-use RF-delivery catheter that houses 4 needle electrodes. A single-use, gel-type patient return electrode completes the RF circuit. It delivers low power (5 Watt) thermal energy at 65°C–85°C. The generator has an integrated irrigation pump to cool the mucosal tissue during therapy and a colour display to guide the user through equipment setup and the treatment procedure. The catheter consists of an inflatable and flexible balloon-basket with 4 needle electrodes positioned radially at 90° angles from one another around the balloon. Electrode tip and surface tissue temperatures are measured by thermocouples in the tip and base of the electrode respectively. The operator controls energy delivery through a footswitch.

To begin treatment, the distance to the gastro-oesophageal junction is measured using an endoscope and then a guide wire with a flexible tip is passed through the endoscope into the stomach, where it stays during the treatment session. The endoscope is withdrawn and the RF-delivery catheter is inserted, following the guide wire. The manufacturer recommends that Stretta Therapy is carried out at 6 different points in the oesophagus: 4 across the lower oesophageal sphincter muscle, 1 at the gastro-oesophageal junction, and 1 in the gastric cardia. Typically, Stretta Therapy takes less than 1 hour and the person returns to normal activity the next day.

## *The innovation*

The Stretta System is the only RF energy device indicated for treating GORD. Stretta Therapy is a minimally invasive procedure that can be done as an outpatient or day case procedure.

## *Current NHS options*

The NICE guideline on [gastro-oesophageal reflux disease and dyspepsia in adults](#) recommends lifestyle modifications such as weight reduction or smoking cessation, and gastric acidity-lowering medication to improve symptoms. People whose symptoms do not respond to medication or lifestyle changes, who develop complications despite medication, or who develop intolerance to medication may be considered for anti-reflux surgery. Most often this is laparoscopic or open fundoplication, but alternative interventional procedures which are covered by NICE guidance are available: [laparoscopic insertion of a magnetic bead band](#) such as LINX, [endoluminal gastroplication](#), or [electrical stimulation of the lower oesophageal sphincter](#).

NICE interventional procedures guidance on [endoscopic radiofrequency ablation for gastro-oesophageal reflux disease](#) recommends that the procedure should only be used with special arrangements for clinical governance, consent and audit or research. This is because, although the evidence on the safety of the procedure is adequate in the short and medium term, there is uncertainty about longer-term outcomes. In addition, there is evidence of symptomatic relief but objective evidence on reduction of reflux is inconclusive.

The [Society of American Gastrointestinal and Endoscopic Surgeons \(SAGES; 2013\)](#) recommends Stretta Therapy for people 18 years and over with GORD: who have had symptoms of heartburn, regurgitation, or both for 6 months or more; whose condition has been partially or completely responsive to medication; and who have declined laparoscopic fundoplication.

NICE is unaware of other CE-marked RF devices used for treating GORD.

## *Population, setting and likely place in therapy*

According to the [manufacturer](#), Stretta Therapy is indicated for adults with GORD if: conservative treatment options have failed; they are concerned about the risks of long-term medication; surgery is unsuitable for them; or they do not want to have invasive surgery. The manufacturer describes Stretta Therapy as a treatment that fits between medicine and surgery and does not prevent a patient having more invasive options in the future if needed.

The manufacturer states that Stretta Therapy should not be used in people who: are under 18 years; pregnant; without GORD; with a hiatal hernia more than 2 cm in size, with achalasia or incomplete lower oesophageal sphincter relaxation in response to swallowing; or who are not suitable for surgery (American Society of Anesthesiologists [ASA] classification IV).

Stretta Therapy is typically carried out under sedation, in an endoscopy suite. It can also be done with general anaesthesia as a day case procedure, depending on patient or centre preference. The procedure is done by a gastroenterologist or upper gastrointestinal surgeon trained in using the Stretta System.

## Costs

### Device costs

**Table 1 Prices of standard components (excluding VAT)**

Component	Price	Other information
Stretta RF-delivery catheter	£2,495	Single use.
RF generator	£25,000	Reusable (anticipated lifespan of 5 years or 1,000 uses).
Compatible patient return electrode (third party)	£4.04 ( <a href="#">NHS Supply Chain</a> )	Single use.
Training	Free of charge	Includes web-based, hands-on, and supervised training during the first 6 procedures.
Maintenance	Done in-house	Includes annual safety testing and checking RF output level.

### Costs of standard care

The [REFLUX Health Technology Assessment](#) (2008) estimated a mean (standard deviation) cost of laparoscopic Nissen fundoplication of £2,787 (£175) based on a survey of 5 UK centres. Variation in costs between centres was caused by differences in staffing and use of disposables.

No information on the NHS costs of alternative therapeutic endoscopic procedures for GORD was found in the public domain.

### Resource consequences

A literature search was carried out to identify any relevant cost or resource evidence for the technology.

The literature search identified 3 economic studies on Stretta Therapy, all done outside the UK.

[Funk et al. \(2015\)](#) developed a Markov model with a 30-year time frame, which predicted that treatment with proton pump inhibitor (PPI) drugs (twice-daily low-dose omeprazole) would have the lowest cost-effectiveness ratio (\$541 per quality-adjusted life year [QALY] gained; American dollars), followed by Stretta Therapy (US\$642/QALY), laparoscopic Nissen fundoplication (LNF; US\$716/QALY) and endoscopic fundoplication (EsophyX; \$1,067/QALY) over a 30-year time frame. At a 6-month cost of \$204 for PPI, sensitivity analyses showed that PPI was the cheapest treatment option, with Stretta and LNF being cost-effective treatments. Stretta was not the most cost-effective treatment because the study assumed a failure rate of Stretta at a probability of 0.205 every 6 months. All Stretta procedures were assumed to occur in an outpatient endoscopy suite under conscious sedation, and the purchase cost of the Stretta System was not included in the model.

The Markov model by [Comay et al. \(2008\)](#) showed that if symptom-free months (SFM) were used as a measure of effectiveness, daily PPI therapy cost the least (\$40/SFM, Canadian dollars) when compared with Stretta Therapy (\$57/SFM) and LNF (\$127/SFM) over a 5-year time frame. When efficacy was measured in QALYs, PPI therapy still had the lowest cost-effectiveness ratio.

The decision tree model applying a cost minimisation approach by [Harewood and Gostout \(2003\)](#) found that PPI therapy was the most economical strategy in patients needing once-daily treatment. PPI therapy was also most economical in patients needing twice-daily medication up to 17 months and beyond 29 months. Between 17 and 29 months, endoluminal gastroplication (using the Endocinch device, which is no longer manufactured) was marginally cheaper than Stretta Therapy.

A retrospective cost analysis of pre- and post-treatment medical claims by [Gregory et al. \(2016\)](#) found that Stretta Therapy was cost saving up to 12 months post-procedure when compared with medical management and fundoplication.

The UK supplier of the Stretta System states that it is currently used in 10 NHS Trusts.

## *Regulatory information*

The Stretta catheter and reusable RF generator were both CE marked to Mederi Therapeutics as Class IIb devices in 2009. The Stretta System is supplied by CJ Medical in the UK.

A search of the [Medicines and Healthcare Products Regulatory Agency](#) website revealed that no manufacturer Field Safety Notices or Medical Device Alerts have been issued for this technology.

## Equality considerations

NICE is committed to promoting equality, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. In producing guidance and advice, NICE aims to comply fully with all legal obligations to: promote race and disability equality and equality of opportunity between men and women, eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, marriage and civil partnership, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief (these are protected characteristics under the Equality Act 2010).

Stretta Therapy is contraindicated in people under 18 years and in pregnancy. Symptoms of GORD are common in pregnant women. Age and pregnancy are protected characteristics under the Equality Act 2010.

## Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the published process and methods statement. This briefing includes the most relevant/best publicly-available evidence relating to the clinical and cost effectiveness of the technology. The literature search strategy, evidence selection methods and detailed data extraction tables are available on request by contacting [medtech@nice.org.uk](mailto:medtech@nice.org.uk).

### *Published evidence*

The results of 1 systematic review (which included 2 randomised controlled trials [RCTs] and 18 cohort series), 2 additional RCTs, 1 non-randomised comparative study and 4 case series, all using the Stretta System, were assessed in the development of NICE interventional procedures guidance on [endoscopic radiofrequency ablation for gastro-oesophageal reflux disease](#). The systematic review and meta-analysis by [Perry et al. \(2012\)](#) was the only one of these studies to report objective physiological measurements after Stretta Therapy.

Of the 14 interventional studies using Stretta Therapy that have been published since the NICE guidance, 1 systematic review ([Lipka et al. 2015](#)) and 5 non-randomised comparator studies ([Hu et al. 2015](#); [Hu et al. 2014](#); [Liang et al. 2015](#); [Liang et al. 2014](#); [Yan et al. 2015](#)) have been included in this briefing.

Table 2 summarises the clinical evidence as well as its strengths and limitations.

**Table 2: Summary of selected studies**

Study	Details of intervention and comparators	Outcomes	Strengths and limitations
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<p><u>Lipka et al. (2015)</u> Systematic review: 4 RCTs; 153 patients with GORD; follow-up ranging from 6–12 months. Multi-centre (Belgium, Egypt, France, US).</p>	<p>3 RCTs: Stretta Therapy versus sham. 1 RCT: Stretta versus PPI therapy. Stretta used in 81 patients.</p>	<p>Study shows no significant difference in physiological parameters including time spent at pH less than 4 over 24 hours, mean lower oesophageal sphincter pressure, ability to stop PPI therapy, and health-related quality of life between Stretta Therapy and control arms.</p>	<p><u>The Society of American Gastrointestinal and Endoscopic Surgeons</u> formally disagreed with the methodology used and conclusions reached. The quality of evidence from RCTs on the efficacy of Stretta was very low. The studies included in the meta-analysis had different comparators and endpoints. The study states that its senior author is a consultant for Endostim, a competing technology. Each included study met its primary endpoint but the meta-analysis concluded that there were no</p>
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			significant improvements in patient outcomes.
<p><u>Hu et al. (2015)</u> Non-randomised comparative study: 137 patients with GORD and severe asthma; 5-year follow-up. Single centre (China).</p>	<p>Stretta Therapy (n=82) versus LNF (n=55).</p>	<p>Significant improvement in symptom scores from baseline were seen in both groups. LNF resulted in significantly better improvements in digestive, respiratory and ENT symptom scores at 1-year and 5-year follow-up when compared with Stretta Therapy.</p>	<p>Non-randomised, uncontrolled, non-blinded study based on a select patient group. No physiological measurements recorded. No statistical comparison of complications.</p>
<p><u>Hu et al. (2014)</u> Non-randomised comparative study: 57 patients with GORD-related childhood-to-adult persistent asthma. Single centre (China).</p>	<p>Stretta Therapy (n=24) versus LNF (n=33, 2 of whom previously had Stretta).</p>	<p>Significant improvement in symptom scores from baseline across pooled results (not able to separate LNF from Stretta). LNF resulted in significantly better improvement in oesophageal symptoms when compared with Stretta Therapy.</p>	<p>Non-randomised, uncontrolled, non-blinded study based on a select patient group. No physiological measurements recorded. No statistical comparison of complications or patient satisfaction between groups, unable to separate some pooled results.</p>

<p><u>Liang et al. (2015)</u> Non-randomised comparative study: 125 patients with GORD completed 3-year follow-up. Multi-centre (China).</p>	<p>Stretta Therapy (n=60) versus LTF (n=65).</p>	<p>Significant improvement in symptom scores from baseline seen in both groups. LTF resulted in significantly better improvements in typical symptoms and a lower revision rate than with Stretta Therapy. There was no significant difference between groups in the proportion of patients no longer needing PPI treatment. Complication rate at 1- and 3-year follow-up was higher for LTF but did not reach significance.</p>	<p>Non-randomised, not controlled. No physiological measurements recorded.</p>
<p><u>Liang et al. (2014)</u> Non-randomised comparative study: 179 patients with GORD completed 5-year follow-up. Multi-centre (China).</p>	<p>Stretta Therapy (n=92) versus LNF (n=87).</p>	<p>Significant improvement seen in symptom scores from baseline in both groups. LNF resulted in significantly better symptom improvements than Stretta Therapy. Significantly more patients having LNF no longer needed PPI treatment than in the Stretta group. Significantly more abdominal distension complications were seen in the LNF group than in the Stretta group.</p>	<p>Non-randomised, not controlled. No physiological measurements recorded.</p>

<p><u>Yan et al. (2015)</u> Non-randomised comparative study: 90 patients with GORD-related extra-oesophageal symptoms reaching 3-year follow-up. Multi-centre (China).</p>	<p>Stretta Therapy (n=47) versus LTF (n=51).</p>	<p>There were significant improvements in symptom scores from baseline in both groups. Improvements in cough, sputum and wheezing symptom scores were not significantly different between groups, but the LTF group had a significantly lower globus score at 3 years. The LTF group reported higher quality-of-life scores than the Stretta group.</p> <p>There was no significant difference between the groups in the proportion of patients no longer needing PPI treatment.</p>	<p>Non-randomised, not controlled. No physiological measurements recorded. Only PPI drug use was recorded.</p>
<p>Abbreviations: ENT, ear nose and throat; GORD, gastro-oesophageal reflux disease; LNF, laparoscopic Nissen fundoplication; LTF, laparoscopic Toupet fundoplication; PPI, proton pump inhibitor; RCT, randomised controlled trial.</p>			

### *Strengths and limitations of the evidence*

None of the reviewed evidence was set in the UK, so this may limit the generalisability of the study findings to NHS settings.

None of the studies compared Stretta Therapy with other therapeutic endoscopic procedures. Five non-randomised comparative studies compared Stretta Therapy with laparoscopic surgery, which could cause population bias because patients for whom surgery was not suitable may have had comorbidities that contributed to outcomes. The systematic review compared Stretta Therapy with either a sham device or PPI therapy and found no significant difference in results.

Four of the 6 reviewed studies focused on PPI therapy independence as an outcome measure, but none recorded the use of other acid reflux medications, such as H<sub>2</sub>-receptor antagonists or antacids. Only 1 study investigated the outcomes of single compared with multiple treatments using Stretta.

The 2 available meta-analyses of Stretta reached contradicting conclusions on the effectiveness of Stretta therapy. Both analyses included studies with a range of inclusion criteria and clinical end-points. The Lipka (2015) meta-analysis was smaller (4 studies; n=153), compared with the Perry (2012) meta-analysis (20 studies; n=1,441).

The most recent cost analysis by Gregory et al. (2016) found that Stretta Therapy was cost saving over medical and fundoplication treatment. This contradicts the findings from 3 previous economic studies, which all found that medical management was the most cost-effective treatment for GORD.

### *Recent and ongoing studies*

Two ongoing trials on Stretta Therapy for GORD were identified in the preparation of this briefing:

- [Stretta in reflux uncontrolled by PPI \(SIRUP\)](#)
- [Management of reflux after sleeve using Stretta \(MaRSS\)](#)

The manufacturer also identified a meta-analysis that is currently in development (unpublished at the time of publication of this briefing). Specialist commentators also identified emerging data not yet in the public domain from recent or ongoing studies.

### **Specialist commentator comments**

Two specialist commentators recommended that a careful, multi-disciplinary approach should be taken to assess which people could be offered Stretta Therapy. The team should include gastroenterologists, gastrointestinal physiologists and gastrointestinal surgeons. One specialist commentator also stated that patients should have an endoscopy and oesophageal physiological measurement before Stretta Therapy, in the same way that people having surgical treatment are prepared.

One specialist commentator noted that the published evidence does support the use of Stretta Therapy in a limited group of people, but the exclusion criteria rule out most people who are referred for treatment of reflux.

There is still uncertainty about the hospital setting for the Stretta procedure. Three specialist commentators stated that in the NHS, Stretta Therapy would be done in the outpatient endoscopy suite, and another said that the setting for the procedure would be determined by clinical preference and centre infrastructure. One commentator felt that it should only be used in specialist centres, with experienced operators who are certified to use it after proper training and clinical governance approvals in their trusts. Another specialist commentator said that conscious sedation in an outpatient endoscopy suite setting is typically preferred because of the lower cost of sedation compared with general anaesthesia, and patient preference and convenience. But another specialist commentator noted that deep sedation would be used for Stretta Therapy in the UK. One

specialist commentator carries out the procedure using total intravenous anaesthesia, with patient recovery in the endoscopy suite and discharge about 3–4 hours after the procedure.

One specialist commentator reflected that Stretta Therapy was not difficult to do, compared with endoscopic resection or peroral endoscopic myotomy, but highlighted that meticulous attention to detail was needed to perform this procedure. This specialist commentator noted that response to Stretta is not immediate, and people are usually reassessed 3 months post-procedure.

One specialist commentator noted controversy around the mode of action of Stretta, particularly because of the lack of physiological evidence. But another specialist commentator felt that the main aims of Stretta Therapy were to treat symptoms, improve quality of life, and reduce reliance on PPI therapy, and that normalising abnormal physiology was not an important measure of success.

One specialist commentator reflected that the complications of Stretta Therapy reported in the literature (that is, pharyngeal pain and retrosternal discomfort) are common to other therapeutic endoscopic procedures on the oesophagus and are typically short-lived. But another specialist commentator noted that there is no data on whether the injury and 'bulking' of the cardiac muscle compromises future surgery if the effect of Stretta does not last.

One specialist commentator was aware of an ongoing (unpublished) single-centre cohort study of Stretta procedures being done in the UK.

## Patient organisation comments

The patient organisation Action Against Heartburn commented that reflux is a very common complaint, but when it is persistent and longstanding there should be careful investigation to find the underlying causes. This is especially important for conditions such as Barrett's oesophagus, which can develop into oesophageal adenocarcinoma. The organisation stated that there is concern about the long-term effects of PPI medication on some people, despite their short-term effectiveness, and also concern about patients for whom PPI medication does not resolve symptoms. People would benefit from devices to help with GORD being available, provided they are safe, comfortable and effective.

## Specialist commentators

Comments on this technology were invited from clinical experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

The following clinicians contributed to this briefing:

- Anjan Dhar (Consultant Gastroenterologist, County Durham and Darlington NHS Foundation Trust – no conflicts)
- Nick Hayes (Consultant Upper Gastrointestinal Surgeon, The Newcastle upon Tyne Hospitals NHS Foundation Trust – no conflicts)
- Jamal Hayat (Consultant Gastroenterologist, St George's Hospital – no conflicts)
- Howard Smart (Consultant Gastroenterologist, The Royal Liverpool and Broadgreen University Hospitals NHS Trust – no conflicts)

Representatives from the following patient organisation contributed to this briefing:

- Action Against Heartburn

## Development of this briefing

This briefing was developed for NICE by Newcastle and York External Assessment Centre. The [Interim process and methods statement](#) sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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