National Institute for Health and Care Excellence

IP 1183 – Insertion of endobronchial nitinol coils to improve lung function in emphysema

Consultation Comments table

IPAC date: Thursday 13 November 2014

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 1: NHS Professional	**1 & Overview**	The committee, I suspect, did not have at the time of discussion the new study by Deslee et al (Thorax 2014) in which high degree of effectiveness in all subjective and objective measurement. The study also showed a good safety profile were demostrated in 60 patients after 12 months. Could the committee examine this study when they meet again?	**Thank you for your comment.** Deslee (2014) was published after the IP team had conducted literature searches, in April 2014, and was not considered in initial deliberations. It has now been added to Table 2.
2	Consultee 2: Specialist society	**1**	The British Thoracic Society welcomes the guidance on this procedure and notes that the recommendations are appropriate.	**Thank you for your comment.** Consultee agrees with committee recommendations
3	Consultee 4 Specialist society	**1**	The RCP is grateful for the opportunity to comment. We wish to endorse the comments submitted by the British Thoracic Society.	**Thank you for your comment** Consultee agrees with committee recommendations.

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4	Consultee 3: Private sector professional on behalf of the manufacturer	**1**	A paper by Hartman J et al reporting the long-term follow-up after bronchoscopic lung volume reduction treatment with coils in patients with severe emphysema has just been accepted for publication by Respirology. The paper reports long-term follow-up of lung volume reduction coil treatment in 38 patients with severe emphysema (median age 59 years, FEV1 27% predicted) who were previously treated in LVR-coil clinical trials. Safety was evaluated by chest X-ray and recording of adverse events; efficacy by pulmonary function testing, 6MWD and questionnaires. Thirty-five patients were followed-up at 1 year, 27 at 2 years and 22 at 3 years. No coil migrations were observed. At 1 year follow-up, all clinical outcomes significantly improved compared to baseline. At 2 years, RV% predicted, mMRC and the SGRQ score were still significantly improved. At 3 years, a significant improvement in mMRC score remained, with 40% of the patients achieving a clinically important difference (MCID) in 6MWD and 59% for the SGRQ. The authors concluded that coil treatment is safe in the long term, with no late pneumothoraces, coil migrations or unexpected adverse events. We can make available this academic-in-confidence data on request.	**Thank you for your comment.** The Hartman (2014) study has been added to Table 2 of the overview.

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5	Consultee 3: Private sector professional on behalf of the manufacturer	**1**	With the addition of these papers, the wording of paragraph 1.1 should be reviewed. On the basis of the updated evidence base and the reported results, we consider that the appropriate wording should be similar to that in the IPG on endobronchial valves (EBVs) in lung volume reduction in emphysema (IPG#465, September 2013): Current evidence on the efficacy of insertion of endobronchial valves for lung volume reduction in emphysema shows some clinical and quality-of-life benefits. Evidence of safety in the short term is adequate but the evidence of safety in the longer term is inadequate in quantity. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research.	**Thank you for your comment.** The Committee considered the proposed new evidence as well as studies identified in the update literature search and retained the initial IPAC recommendations. The committee felt that quality of life and relief of breathlessness (dyspnoea) were important outcome measures in section 1.2 that would inform any future review of the procedure. A Committee comment has been added to section 6 to highlight that: “The Committee noted that emphysema is a common and progressive condition. For most patients with distressing symptoms there is the possibility of established surgical treatments, but if further evidence supports the efficacy of insertion of endobronchial coils this procedure could provide a less invasive treatment option.”

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6	Consultee 3: Private sector professional on behalf of the manufacturer	**2**	The text of paragraph 2.2 should be amended to include endobronchial coils as a treatment option. Neither the guidance nor the overview describe the rationale for endobronchial nitinol coils. Bronchoscopic lung volume reduction using one-way EBVs is only successful in patients with no inter-lobar collateral ventilation, who have heterogeneous rather than homogeneous emphysema, and require than all airways into the target lobe are blocked, which can be technically difficult. Two-thirds of patients with severe emphysema have collateral ventilation between the target lobe and adjacent lobes (Shah PL and Herth FJ. Current status of bronchoscopic lung volume reduction with endobronchial valves. Thorax, 2013;69(3):280-6): for these patients, EBVs are unlikely to provide any clinical benefit. A large proportion of severe emphysema patients cannot be effectively treated with EBVs, are not fit enough to undergo lung volume reduction surgery, and cannot have a lung transplant because of a short of donor organs. In assessing the evidence base, the committee should take account of the fact that this procedure is an option for a group of patients for whom current treatments are inadequate, inappropriate, or impractical.	**Thank you for your comment.** The IP programme does not routinely include the procedure which is being assessed in section 2.2 of the guidance: Indications and current treatments section. Lung volume reduction using one-way endobronchial valves has been added to section 2.2 as a possible treatment option for emphysema. IP procedure descriptions do not routinely discuss the limitations of comparator treatments. Committee comments have been added to section 6 to highlight that: 1. The Committee noted that emphysema is a common and progressive condition. For most patients with distressing symptoms there is the possibility of established surgical treatments, but if further evidence supports the efficacy of insertion of endobronchial coils this procedure could provide a less invasive treatment option. 2. The Committee noted that this procedure may be used in some patients for whom lung volume reduction surgery and insertion of endobronchial valves are not suitable.

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7	Consultee 3: Private sector professional on behalf of the manufacturer	**2**	The committee may also wish to note that lung volume reduction surgery in patients previously reported to be at high risk and those with non “upper-lobe emphysema and high base-line exercise capacity are poor candidates for lung-volume “reduction surgery, because of increased mortality and negligible functional gain (National Emphysema Treatment Trial Research Group. A randomized trial comparing lung-volume “reduction surgery with medical therapy for severe emphysema. NEJM 2003;348(21):2059-73).	**Thank you for your comment.** A Committee comment has been added to section 6 to highlight that: “The Committee noted that this procedure may be used in some patients for whom lung volume reduction surgery and insertion of endobronchial valves are not suitable”
8	Consultee 1: NHS Professional	**3**	In our institution there are over 90 patients who have been worked out for lung volume reduction in a regular MDT team as suggested by NICE. Out of those there are 53 patients who have incomplete lobe fissure or homogenous emphysema and therefore could not be treated by intrabronchial valve, but have enough lobe tissue to be eligible for emphysema coil. Currently, endo-bronchial coil would be a credible treatment	**Thank you for your comment.** A Committee comment has been added to section 6 to highlight that: “The Committee noted that this procedure may be used in some patients for whom lung volume reduction surgery and insertion of endobronchial valves are not suitable”

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9	Consultee 3: Private sector professional on behalf of the manufacturer	**3**	The text of paragraph 3.1 is not consistent with the current IFU for the device: The [redacted] LVRC System is intended to improve lung function in patients with upper and/or lower lobe heterogeneous emphysema and/or with multiple emphysematous lobes with focal tissue defects.• The text should be amended to be consistent with the IFU. The Committee may also wish to note that BSI, the notified body responsible for CE-marking of lung volume reduc tion coils has just accepted the following revised indication: The RePneu Coil system is intended to improve exercise capacity, lung function, and quality of life in patients with both heterogenous and homogenous emphysema.•	**Thank you for your comment.** The text in paragraph 3.1 has been changed to: “The procedure is intended to improve lung function in patients with upper or lower lobe heterogeneous emphysema, as well as patients with multiple emphysematous lobes with focal tissue defects”
10	Consultee 3: Private sector professional on behalf of the manufacturer	**3**	The text of paragraph 3.2 is slightly misleading. Typically up to 10 coils are used in each lobe treated, and patients normally undergo a second procedure to treat the other lung. The Committee may wish to amend the text.	**Thank you for your comment.** The text in paragraph 3.1 has been changed to: “Typically, 5 to 15 coils are inserted in each treated lobe and each lung is treated in separate procedures”

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11	Consultee 3: Private sector professional on behalf of the manufacturer	**4 & 5**	The overview and guidance should be updated to include the paper by Deslee et al (Deslee G et al. Lung volume reduction coil treatment for patients with severe emphysema: a European multicentre trial. Thorax; 2014 Jun 2. pii: thoraxjnl-2014-205221. doi: 10.1136/thoraxjnl-2014-205221. [Epub ahead of print]. NCT trial number NCT01328899) presents the results of a prospective non-comparative study of n = 60 patients (n = 115 procedures in which n = 1125 LVR coils were placed).	**Thank you for your comment.** Deslee (2014) was published after the IP team had conducted literature searches, in April 2014, and was not considered in initial deliberations. It has now been added to Table 2.

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12	Consultee 3: Private sector professional on behalf of the manufacturer	**4**	Sections 4 (Efficacy) and 5 (Safety) should be reviewed. The overview and guidance should be updated to include the Deslee et al and Hartman et al papers. While recognising that the Committee has not undertaken a comparative review of endobronchial nitinol coils vs EBVs for lung volume reduction in severe emphysema, there is an overlap in the target patient population and EBVs are recognised in the overview as being a comparative treatment. IPAC has recently (September 2013) issued guidance on EBVs for lung volume reduction. The committees guidance on endobronchial nitinol coils should be broadly consistent with its views on EBVs, in respect of efficacy and safety. The findings in the papers reviewed in the overview for endobronchial nitinol coils are very comparable with those reviewed in the overview for EBVs. For example, SGRQ, 6MWT, and FEV1 outcome measures are as good or better for endobronchial nitinol coils and the safety profile is as good or better (for example, in terms of device migration, deaths, LRTIs etc).. Between 5% and 7% of EBVs migrate, are aspirated, or expectorated: no similar events have been reported in studies of endobronchial nitinol coils. On this basis, we consider that the committee proposed guidance that endobronchial nitinol coils be used in research only is unreasonably restrictive given the published evidence. Research only guidance is not warranted by the available data, restricts access to a therapeutic option to patients for whom current treatments are ineffective, inappropriate, or impractical; and given the data available to IPAC on EBVs, is inconsistent with IPG465.	**Thank you for your comment.** Deslee (2014) was published after the IP team had conducted literature searches, in April 2014, and was not considered in initial deliberations. It has now been added to Table 2. The Hartman (2014) study has also been added to Table 2 of the overview. **Please refer to comment 6.**

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13	Consultee 3: Private sector professional on behalf of the manufacturer	**4**	One specialist adviser highlighted that current trials lacked adequate blinding and used quality of life as a primary end point and considered that might be inappropriate because of a potentially high placebo effect. The committee should be aware that double blinding a procedure involving a medical device that needs radiological assessments is impossible. In the Shah RCT all follow-up assessments were performed by research nurses and physiologists who were blinded to the treatment the patient had received. We are not clear why quality of life outcome measures might be considered inappropriate. Lung function is a surrogate endpoint; none of the treatments for severe emphysema (with the possible exception of lung transplantation) are curative and the principal aim of treatment with endobronchial nitinol coils and alternative treatments is to improve quality of life.	**Thank you for your comment.** The committee considers all concerns about efficacy that are highlighted by specialist advisers.

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14	Consultee 3: Private sector professional on behalf of the manufacturer	**4**	In relation to Herth 2010, the overview states that a study design issue was that the study was neither designed nor powered to evaluate a statistical significance in clinical outcomes between groups. In fact, no p values are reported (as the overview itself states), and no statistical analysis is presented. The text of section 4 makes no reference to either Herth 2010 or Klooster 2014, both of which are included in the overview analysis. The guidance should also be reviewed in the light of the evidence now available to the Committee (e.g. Desless 2014 and Hartman 2014).	**Thank you for your comment.** The overview highlights that authors (Herth, 2010) stated that the study was neither designed nor powered to evaluate a statistical significance between groups. The majority of evidence reported in the guidance document is obtained from the only randomised controlled trial available. Deslee (2014) and Hartman (2014) have been added to the overview and are briefly mentioned in the guidance document. Herth (2010) and Klooster (2014) are case series included in the more-detailed overview. The guidance document highlights the key findings from available literature and tends not to repeat similar outcomes reported by multiple studies included in the overview. Furthermore, a web-link conferring access to the full evidence reviewed by the Committee is provided in the guidance.

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15	Consultee 3: Private sector professional on behalf of the manufacturer	**5**	Although specialist advisers highlighted haemorrhage, coil migration, pneumomediastinum, respiratory failure and erosion of coils into major vessels as theoretical adverse events, the committee should note that haemorrhage is extremely rare, migration of coils has not been reported, pneumomediastinum has never been observed, the data do not suggest higher incidence of respiratory failure post coil treatment, and coil erosion into major vessels has not been reported. One specialist adviser stated that the safety and efficacy of the procedure in patients with coexisting bronchiectasis or patients taking anticoagulants is currently unknown. The committee should note that in accordance with the IFU, coil treatment is not recommended for these patients.	**Thank you for your comment.** The Committee considers all adverse events (including anecdotal and theoretical adverse events) reported by specialist advisers.

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16	Consultee 3: Private sector professional on behalf of the manufacturer	**5**	There is no mention in section 5 to Herth 2010, Klooster 2014, Hartman 2014 which is included in the overview analysis. The guidance should also be reviewed in the light of the evidence now available to the Committee	**Thank you for your comment.** The majority of evidence reported in the guidance document is obtained from the only randomised controlled trial available. Hartman (2014) has been added to the overview and is briefly mentioned in the guidance document. Herth (2010) and Klooster (2014) are case series included in the more-detailed overview. The guidance document highlights the key findings from available literature and tends not to repeat similar outcomes reported by multiple studies included in the overview. Furthermore, a web-link conferring access to the full evidence reviewed by the Committee is provided in the guidance.
17	Consultee 1: NHS Professional	**General**	We believe that there is an unmet need in COPD patients. A parallel group of cardiac patients would be offered interventional treatment that would have inferior outcome to coil treatment. On the same line, British COPD patients are disadvnataged compared to their European patients	**Thank you for your comment.** IP guidance considers one intervention for treating a specific indication; it does not review technologies for a diversity of indications.

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	Consultee 5 Private Sector Professional	**General**	I am Professor of Medicine, [redacted]; Director, Division of Pulmonary and Critical Care Medicine; Chief, Section of Pulmonary Medicine; Director, Medical Intensive Care Unit and Ventilator Rehabilitation Unit; and Co-Director, Center for Inflammation, Translational and Clinical Lung Research. I have done 14 procedures using the coil therapy in patients with advanced homogeneous emphysema. The technique is relatively straightforward to perform with minimum risk to the subject. Patient's overall have shown significant improvement on a case-by-case basis. Overall this represents the only therapy other than lung transplantation to a patient group who otherwise does poorly with medical therapy only. Although further optimization of the therapy is required in terms of number of coils or size of coil, at the present time this therapy offers a significant novel treatment for patients who otherwise have limited therapeutic options.	**Thank you for your comment.**