

National Institute for Health and Care Excellence
IP1973 Intravascular lithotripsy for calcified arteries in peripheral arterial disease

IPAC date: 12th October 2023

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response
1.	Consultee 1 Company Shockwave Medical	Lay description	<p>IVL uses acoustic pressure waves, not ultrasound. Ultrasound waves, generated by piezo electric crystals, are high frequency (1 to 12 MHz) and have equal positive and negative peak acoustic pressures (+ - 2 – 4 MPa). Ultrasound waves propagate through tissue and are absorbed or reflected by tissues of differing acoustic impedance. Reflected ultrasound waves enable diagnostic images to be created and absorbed ultrasound waves generate heat which can be used to ablate targeted tissues.</p> <p>In contrast, acoustic pressure waves generated from IVL spark gap emitters have a low frequency (1 to 2 Hz) and a high positive peak acoustic pressure (around 5 MPa) and a low negative acoustic pressure (around 0.3MPa). The waveform specific to acoustic pressure waves used in IVL does not generate heat when transiting from soft to hard tissue but imparts compressive stress when calcium is encountered which is the primary therapeutic mechanism of calcium fracture. [Kereiakes DJ et al. JACC Cardiovasc Interv 2021;14(12):1275-1292]</p> <p>For accuracy, we suggest a change to this sentence to read “Acoustic pressure waves are generated by spark gap lithotripsy emitters within the balloon, which fracture the calcified plaque, improving vessel compliance and consequently allowing effective therapeutic dilation of the artery.”</p>	<p>Please respond to all comments</p> <p>Thank you for your comment.</p> <p>This summary is intended to be a brief description of the indication and procedure and is aimed at a lay audience.</p> <p>Ultrasound has been changed to acoustic pressure waves.</p>

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2.	Consultee 1 Company Shockwave Medical	Lay description	<p>Stenting is also sometimes used following standard angioplasty and is not part of the IVL procedure. IVL has been shown to reduce the need for stenting compared with standard angioplasty, which preserves the patient's options for future revascularisation if required.</p> <p>We suggest a change to this sentence to reflect this: "The catheter and balloon are removed and, as with standard angioplasty, sometimes a small metal tube, called a stent, is inserted to help keep the artery open.</p>	<p>Thank you for your comment.</p> <p>The committee discussed this comment but decided not to change the lay description. The main procedure description has been changed.</p>
3.	Consultee 1 Company Shockwave Medical	1.5	As IVL is used as part of an existing treatment pathway and used to treat patients with multiple comorbidities, measuring the impact of IVL alone on patient reported outcomes is extremely complex and may not be practically achievable as a research objective.	<p>Thank you for your comment.</p> <p>Section 1.5 has been changed to include details of additional interventions.</p>
4.	Consultee 1 Company Shockwave Medical	1.5	As one of the specialist experts commented at the IPAC meeting on 8 June, a very large RCT would be needed to demonstrate impact of IVL on amputation rate. As such this may not be practically achievable as a research objective.	<p>Thank you for your comment.</p> <p>Section 1.5 does not stipulate that the research should be in the form of randomised controlled trials.</p>
5.	Consultee 1 Company Shockwave Medical	2.3	<p>IVL uses acoustic pressure waves, not ultrasound.</p> <p>To be correct, this sentence should read: "An angioplasty balloon containing a source of acoustic pressure waves (lithotripsy emitters) is introduced and inflated next to the heavily calcified arterial plaques".</p>	<p>Thank you for your comment.</p> <p>Ultrasound has been changed to acoustic pressure waves.</p>
6.	Consultee 1 Company	2.3	<p>IVL uses acoustic pressure waves, not ultrasound. To be correct, this sentence should read: "Acoustic pressure waves are transmitted from lithotripsy emitters within</p>	Thank you for your comment.

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	Shockwave Medical		the balloon, fracturing superficial and deep calcium within the arterial wall".	Please respond to all comments Ultrasound has been changed to acoustic pressure waves.
7.	Consultee 1 Company Shockwave Medical	3.5	<p>Further evidence of IVL on iliac lesions comes from a prospective, real-world, multicentre registry study in 108 patients, where IVL was used to assist transcatheter aortic valve implantation (TAVI) [Nardi 2021]. The presence of severe calcific atherosclerosis at the iliofemoral axis may preclude the transfemoral approach to TAVI. In this study, the target lesion was most often localised at the common and/or external iliac artery (93.5% of cases). Transfemoral aortic valve delivery was successful in 100% of cases.</p> <p>Nardi G, De Backer O, Saia F, et al. Peripheral intravascular lithotripsy for transcatheter aortic valve implantation: a multicentre observational study. <i>Eurointervention : Journal of Europr in Collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology.</i> 2022 Apr;17(17):e1397-e1406</p>	<p>Thank you for your comment.</p> <p>As stated in the overview, studies that used intravascular lithotripsy to allow access for an endovascular cardiac procedure were not included in this review.</p> <p>A committee comment has been added to the draft guidance to clarify that such studies were not included.</p>
8.	Consultee 1 Company Shockwave Medical	General	<p>Additional evidence in the iliac arteries is also provided in a study by Nardi et al, which has not been considered in this evidence review.</p> <p>Further evidence of IVL on iliac lesions comes from a prospective, real-world, multicentre registry study in 108 patients, where IVL was used to assist transcatheter aortic valve implantation (TAVI) [Nardi 2021]. The presence of severe calcific atherosclerosis at the iliofemoral axis may preclude the transfemoral approach to TAVI. In this study, the target lesion was most often localised at the common and/or external iliac artery (93.5% of cases). Transfemoral aortic valve delivery was successful in 100% of cases and the authors concluded that IVL-assisted transfemoral TAVI proved to be a safe and effective approach, which helps to expand the indications for transfemoral TAVI in patients with severe calcific PAD.</p> <p>Nardi G, De Backer O, Saia F, et al. Peripheral intravascular lithotripsy</p>	<p>Thank you for your comment.</p> <p>As stated in the overview, studies that used intravascular lithotripsy to allow access for an endovascular cardiac procedure were not included in this review.</p> <p>A committee comment has been added to the draft guidance to clarify that such studies were not included.</p>

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			for transcatheter aortic valve implantation: a multicentre observational study. Eurointervention : Journal of EuroPCR in Collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology. 2022 Apr;17(17):e1397-e1406	Please respond to all comments
9.	Consultee 1 Company Shockwave Medical	Overview	This study reflects high rates of atherectomy as an adjunct to angioplasty in the US health system and has limited generalisability to the UK patient population and current clinical practice. At the time of the study, the US had reimbursement for atherectomy and not IVL. Many atherectomy's were performed to facilitate a better classification of payment.	Thank you for your comment. The rates of atherectomy are reported in the overview and the validity and generalisability section notes that most studies used intravascular lithotripsy as an adjunct to other procedures. The committee discussed this comment and decided not to change the guidance.
10.	Consultee 1 Company Shockwave Medical	Overview	We question the appropriateness of including a single case report of a common minor procedural complication related to venous access when other higher level evidence describing safety of IVL is available in large observational and randomised controlled trials. We also question the inclusion of this particular single case report and not the many others that are published for IVL. If including this single case report, it should be put into context. The haematoma experienced by the patient is a minor complication common to peripheral interventional procedures rather than a complication specific to IVL.	Thank you for your comment. The case report was included because it described a unique safety event that had not previously been reported in association with intravascular lithotripsy. The rationale for the recommendation of special arrangements in the draft guidance notes that the evidence suggests the procedure is safe.

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