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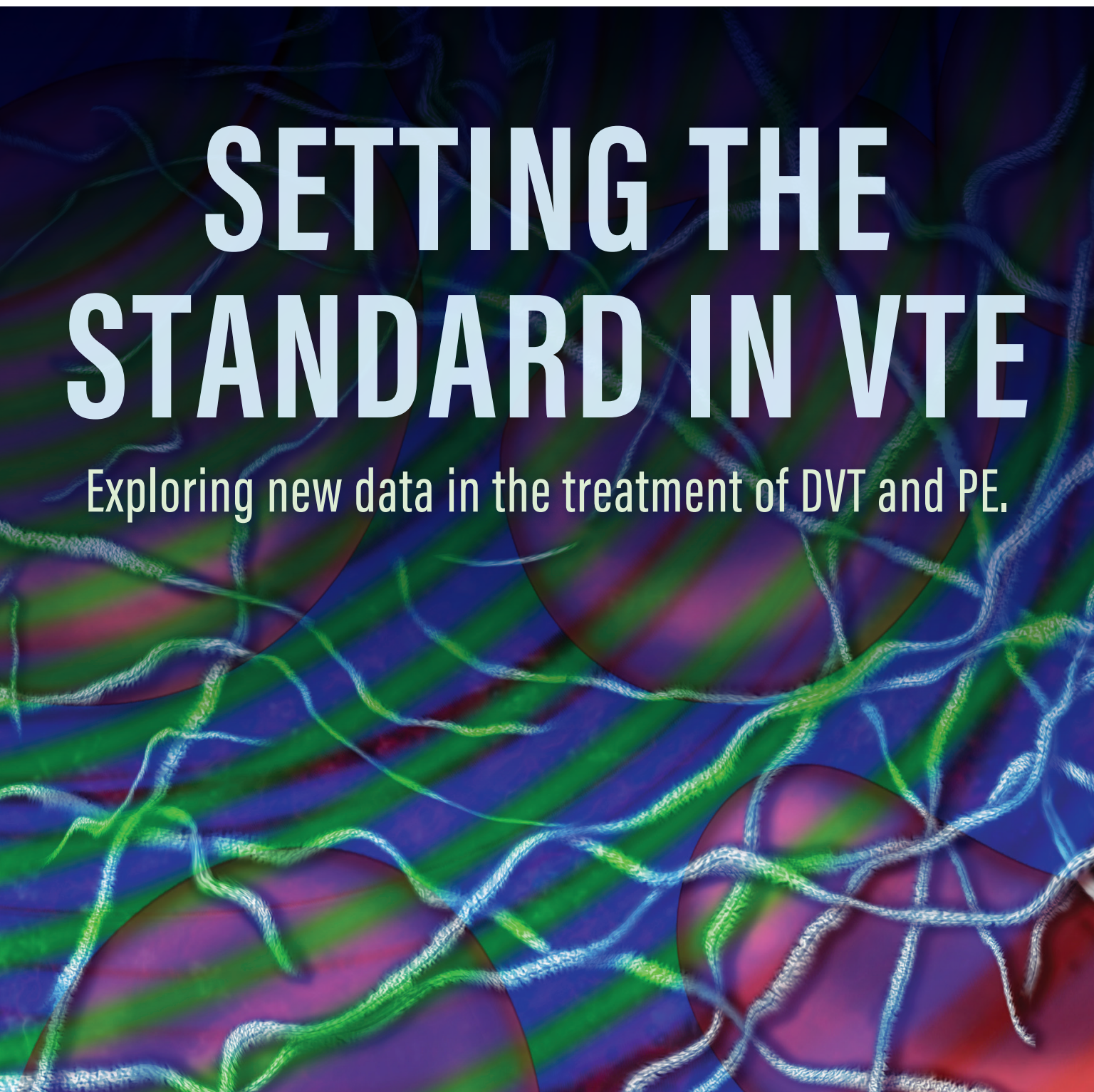
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SETTING THE STANDARD IN VTE

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OPTALYSE PE Demonstrated Significant Improvement in Right Ventricular Size With Shorter Infusion Times and Lower Doses of tPA, Making Ultrasound-Accelerated Thrombolysis Even Safer

BY VICTOR F. TAPSON, MD



The hypothesis of the OPTALYSE PE trial is that less-intensive thrombolytic therapy—shorter infusions and lower doses of thrombolytics—is safer and more advantageous to patients with acute pulmonary embolism (PE) who receive ultrasound catheter-directed therapy. The lower the dose of tissue plasminogen activator (tPA), the lower the risk of major bleeding events, including catastrophic intracranial hemorrhage (ICH). The faster patients' clots are lysed, the less time they spend in the intensive care unit and in the hospital.

In the past, I've found that administering tPA in the range of 10 mg (or urokinase at low doses), pushed through a syringe instead of a drip, over approximately 10 minutes will often resolve a very fresh, large proximal embolus. However, tPA has a short half-life, and the too-short infusion time may be inadequate in many cases. My belief is that at least 2 hours of systemic or catheter-directed therapy should be considered, except in more emergent settings when a patient is deteriorating and may arrest (or has arrested).

My experience suggested that short infusions of low-dose tPA could work to improve right ventricular (RV) function and decrease pulmonary artery pressure. We needed a study to compare low-dose thrombolytic therapy to the "standard" (ULTIMA and SEATTLE II) regimen of approximately 24 mg of tPA over 12 to 24 hours with ultrasound-facilitated, catheter-directed thrombolysis (EKOS® device, BTG International) for intermediate-risk PE. This was the basis of the OPTALYSE PE trial.

OPTALYSE PE, which we presented at the American Thoracic Society International Conference in May 2017, demonstrated that shorter-duration infusions with lower doses of tPA utilizing EKOS® therapy were just as effective as the standard doses utilizing EKOS® therapy, but with a

much lower rate of bleeding. See Figures 1 through 5 for an illustrative case example.

REDUCTION IN RV/LV RATIO IN HALF THE TIME AND DOSE

The OPTALYSE PE study included 101 participants at 17 centers with acute proximal PE in at least one main or proximal lobar pulmonary artery with a right ventricular to left ventricular (RV/LV) end-diastolic diameter ratio ≥ 0.9 on chest CTA.¹ Participants were randomly assigned to one of four ultrasound-facilitated, catheter-directed thrombolysis regimens, which varied in duration and total amount of

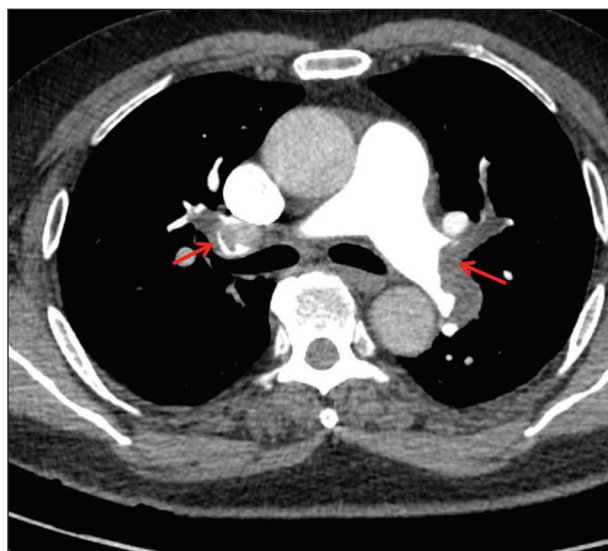


Figure 1. An extensive bilateral PE (arrows). The patient had dyspnea, a heart rate of 120 bpm, and blood pressure of 110/70 mm Hg. Oxygen saturation was 94% on room air. Troponin and BNP were elevated at 2.7 ng/mL and 146 pg/mL, respectively.

tPA. Cohort 1 received 4 mg of tPA (per lung) over 2 hours, cohort 2 received 4 mg of tPA (per lung) over 4 hours, cohort 3 received 6 mg of tPA (per lung) over 6 hours, and cohort 4 received 12 mg of tPA (per lung) over 6 hours. A few patients received therapy to one lung, but the majority received bilateral tPA via a catheter in each lung. All patients also received therapeutic anticoagulation, although the heparin dose was reduced between 300 and 500 U/h during the thrombolytic infusion.

The RV/LV ratio was significantly reduced in all cohorts 48 hours after the procedure, ranging from -0.46 in cohort 1 to -0.48 in cohort 4 (a reduction of 23%–26%). This is consistent with results achieved in SEATTLE II, a large, prospective, single-arm trial in which 24 mg of tPA was given over 12 hours with bilateral catheters.² The mean RV/LV ratio in SEATTLE II participants decreased from 1.55 before the procedure to 1.13 at 48 hours after the procedure (difference, -0.42). Patients in the OPTALYSE PE trial also saw statistically significant improvements in their modified Miller score (embolic burden on CTA), with increasing reductions from cohort 1 (mean change, -5%) to cohort 4 (mean change, -26%).

A LOWER RATE OF BLEEDING EVENTS

The smaller doses of tPA used in OPTALYSE PE appeared to reduce the risk of major bleeding complications (overall major bleeding rate was 3%). In comparison, participants in SEATTLE II, which evaluated the standard regimen of 24 mg of tPA, had a 10% rate of major bleeding (but no fatal bleeding events or ICHs). In OPTALYSE PE, the few major bleeding events occurred only in cohorts 2 and 4. One patient with PE and residual deep vein thrombosis had an excellent response to the 8-mg OPTALYSE PE regimen but developed severe recurrent PE about 24 hours after the EKOS[®] procedure. She received intravenous (IV) tPA at a systemic dose and developed multifocal ICH but completely recovered. Based on the temporal relationships,

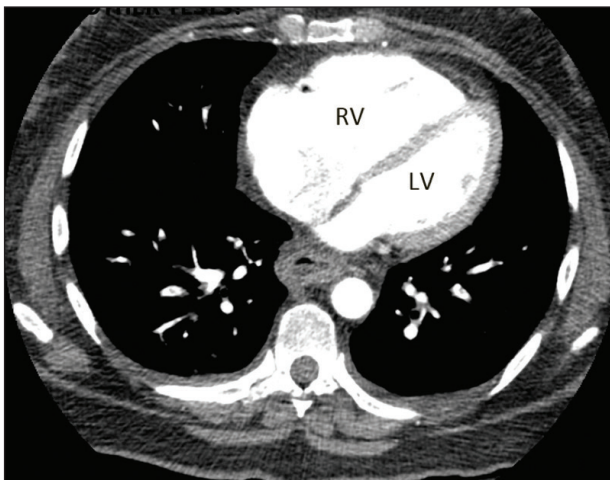


Figure 2. CT showing a dilated right ventricle.

it was highly unlikely that the ICH was related to the very low-dose OPTALYSE PE regimen but rather was related to the IV tPA. A second patient who developed ICH had a prior history of abnormal platelet function and labile hypertension. This was the first reported ICH that may have been EKOS[®]-related in the 277 patients participating in the EKOS[®] PE trials. In contrast, systemic thrombolysis carries a 2% to 3% risk of ICH.³ The ULTIMA, SEATTLE II, and OPTALYSE PE studies confirm that we can effectively lyse clots with EKOS[®] therapy, yet minimize the risk of ICH and other major bleeding.

We sometimes use ultrasound catheter-directed thrombolysis in patients with relative contraindications to higher-dose systemic thrombolysis, such as recent surgery, trauma, or recent bleeding. In such cases, the low-dose, shorter-infusion OPTALYSE PE regimens could be advantageous (patients deemed at high risk for bleeding were excluded from OPTALYSE PE). As patients become more compromised, there is a higher potential for bleeding, and thus more experience and caution are required. For example, a recent gastrointestinal bleed or surgery usually requires rapid and detailed consultation with a specialist (eg, endoscopic surgeon) prior to consideration of a thrombolysis-based plan, even if it is low dose and catheter-based.

More work is still needed in the setting of massive PE. Some high-risk patients were treated with catheter-based therapy in the SEATTLE II trial, but we do not have experience treating high-risk PE using these low-dose, shorter-infusion regimens. However, shorter infusions with less tPA may be effective in treating patients with high-risk PE, particularly those on the less severe end of the spectrum (ie, those who are hypotensive but who stabilize after fluid and low-dose single pressor therapy).

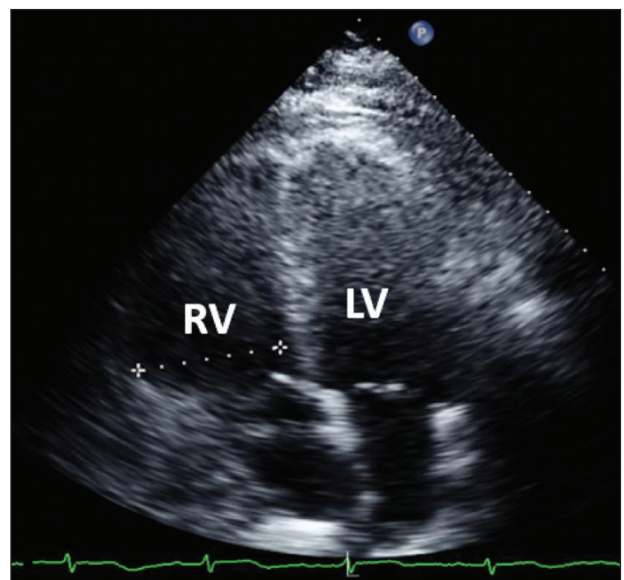


Figure 3. An echocardiogram showing that the right ventricle was dilated and markedly hypokinetic.

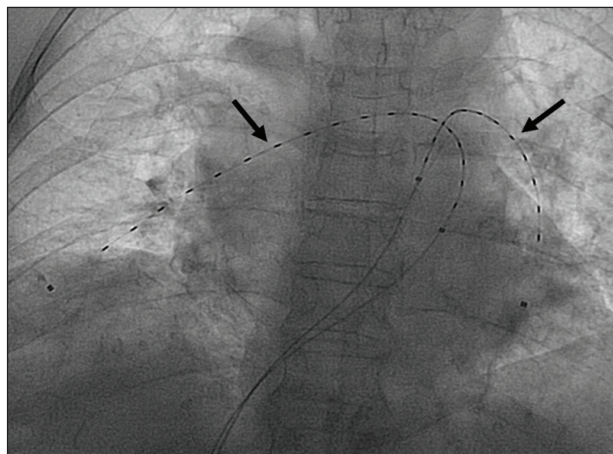


Figure 4. A bilateral ultrasound showing EKOS® catheters in place (arrows).

Based on preliminary OPTALYSE PE data, no single treatment regimen emerged as superior to the others. Although the two lowest doses of 8 mg of total tPA (cohorts 1 and 2) resulted in the smallest but still statistically significant improvement in modified Miller score, we saw a statistically and clinically significant improvement in RV/LV ratio in all four groups. Analyzing additional secondary endpoints of the study may give us a better idea of the most effective dosing regimen. My own clinical experience leads me to favor the cohort 3 regimen (ie, 6-hour infusion of a total of 12 mg of tPA or 6 mg to each lung) to treat intermediate-risk PE. Clinicians may still wish to individualize treatment for patients based on clinical parameters and perceived bleeding risk, but what is clear now is that the standard regimen of 24 mg of tPA over 12 to 24 hours is no longer necessary to achieve optimal results.

WHICH PATIENTS TO TREAT?

All participants in our OPTALYSE PE study had intermediate-risk PE, but some had more concerning parameters, such as an abnormal RV and elevated troponin or brain natriuretic peptide, which can be classified as high-intermediate-risk PE or very severe RV hypokinesis. Other participants were on the other end of the spectrum with intermediate-low-risk PE, characterized by a more mildly abnormal RV or elevated troponin or brain natriuretic peptide. Some clinicians may choose to take all patients with intermediate-risk PE to the interventional radiology or cardiac cath lab, but OPTALYSE PE did not evaluate which intermediate-risk patients should be treated with low-dose, short-duration EKOS® therapy.

To date, most rigorous clinical trial data are derived from catheter-based thrombolysis with the EKOS® device, including the ULTIMA study, which randomized patients with acute PE to EKOS® and heparin or heparin alone.⁴ However, more research is needed to define the optimal EKOS® dosing regimen. Our cohorts were small, and a larger study

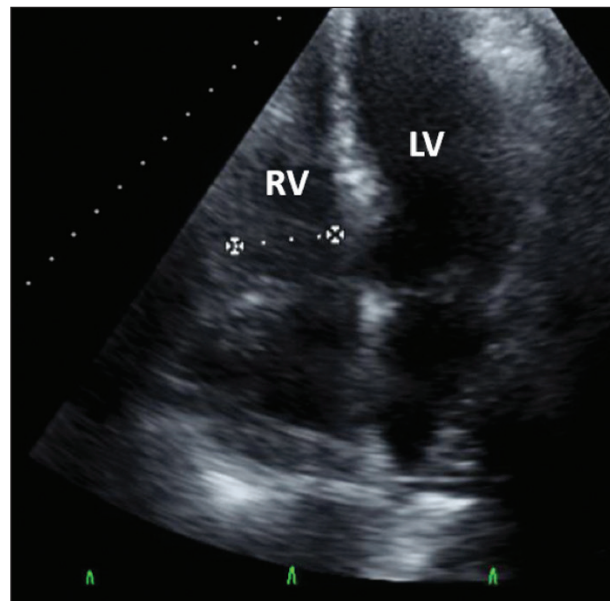


Figure 5. An echocardiogram showing that the right ventricle had significantly improved in size and function by 12 hours after the infusion.

focusing on a few short, low-dose regimens would be valuable, as well as studies that evaluate whether catheter-based therapy improves mortality and in which populations and whether it improves long-term outcomes including chronic thromboembolic disease and pulmonary hypertension.

CONCLUSION

Knowing that we can safely and effectively lyse clots in intermediate-risk PE patients with shorter-duration, lower-dose, ultrasound-accelerated thrombolysis is a major step in advancing PE treatment. We do not need as much tPA or duration of infusion as we once thought—and our patients will benefit from very good outcomes and a safer procedure. ■

1. Tapson VF, Piazza G, Goldhaber SZ, et al. Optimum duration and dose of r-tPA with the acoustic pulse thrombolysis procedure for submassive pulmonary embolism: OPTALYSE PE. Presented at: American Thoracic Society International Conference 2017; May 19–24, 2017; Washington, DC.
2. Piazza G, Hohlfelder B, Jaff MR, et al. A prospective, single-arm, multicenter trial of ultrasound-facilitated, low-dose fibrinolysis for acute massive and submassive pulmonary embolism: the SEATTLE II study. *JACC Cardiovasc Interv.* 2015;8:1382–1392.
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Implementation of the OPTALYSE Study for Submassive Pulmonary Embolism: Patient Selection Criteria and Protocols

BY NOAH J. JONES, MD, FACC, FSCAI



Our hospital was one of the highest-enrolling sites in the OPTALYSE PE trial, which demonstrated that patients with submassive pulmonary embolism (PE) who received Acoustic Pulse Thrombolysis™ (APT or EKOS® therapy, BTG International) using the EKOS® catheter (BTG International) experienced rapid and significant reduction in the right ventricular/left ventricular (RV/LV) ratio and reversal of RV dysfunction, even with doses of the thrombolytic agent as low as 4 mg per catheter.¹ The results of OPTALYSE PE have allowed us to refine our institutional protocols for the treatment of submassive PE in a way that improves outcomes, safety, and patient satisfaction.

OUR EXPERIENCE

We began offering Acoustic Pulse Thrombolysis™ therapy with the EKOS® device in 2011 and have treated more than 350 patients presenting with submassive PE with EKOS®. Before OPTALYSE PE, there was no reported experience on the safety and efficacy of very low-dose and short-duration treatment strategies. Since the early days of the SEATTLE II trial,² our institutional protocol was to adhere to a regimen of 1 mg of tissue plasminogen activator (tPA) administered bilaterally for 12 hours (total of 24 mg), and we were very comfortable with that protocol.

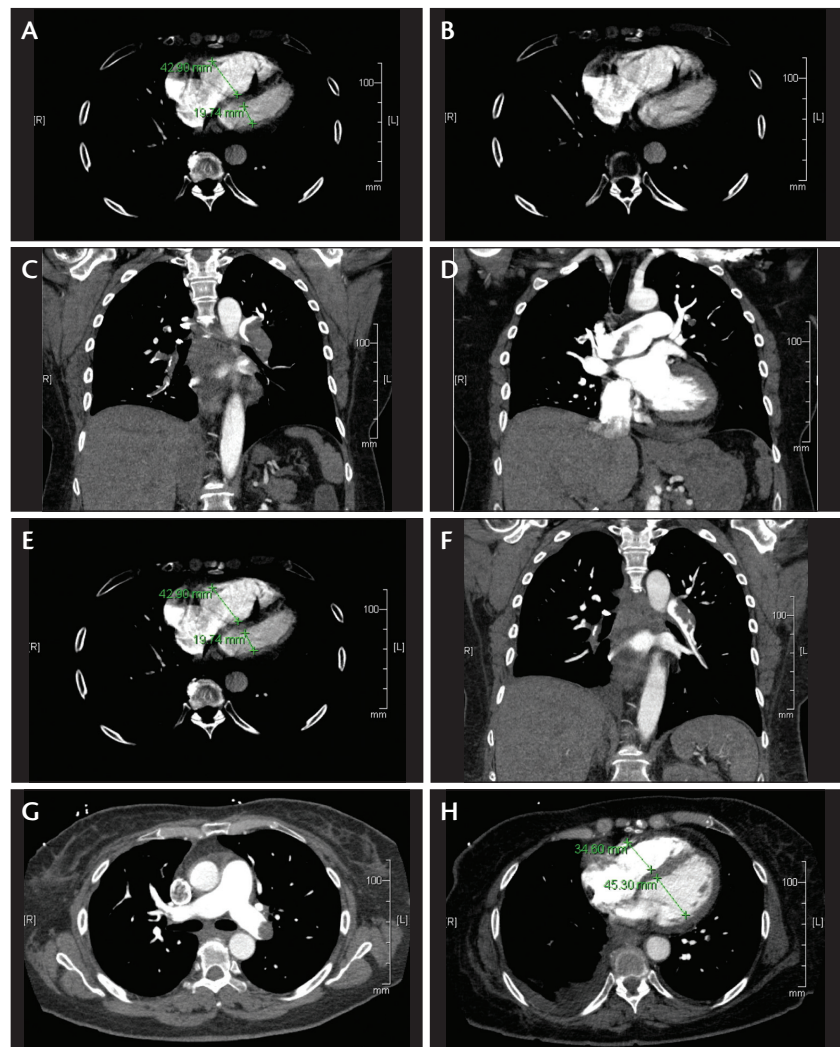


Figure 1. CTA imaging from OPTALYSE PE patient number two, a 59-year-old woman with a history of metastatic breast cancer (currently in remission), deep vein thrombosis, and prior inferior vena cava filter placement. She was experiencing shortness of breath over 3 days. We evaluated her troponin (0.33 ng/mL) and her vitals stabilized. We conducted CTA of the ST and right axis deviation. Before treatment, the RV/LV ratio was 2.17 (E). After OPTALYSE PE protocol of 1 mg per hour per lung over 6 hours for a total of 12 mg of tPA (F–H), RV/LV was 0.76 (H).

However, the results of OPTALYSE PE have given us a variety of new options for treating patients with submassive PE, providing significantly greater flexibility when choosing doses and duration of treatment (Figure 1). At our institution, we have already adopted the 6-hour, 12-mg protocol as an initial strategy, with a plan to extend treatment to a 12-hour duration if we feel it is clinically necessary for the patient. For example, for patients with a higher bleeding risk because of advanced age or recent surgery, we typically choose lower doses and shorter durations of therapy, sometimes < 6 hours. At the other end of the scale, we very rarely exceed a total of 24 mg in a 12-hour dosing.

Risk stratification remains essential when initially evaluating acute PE patients. Many realize that, even within the category of submassive PE, there is a spectrum of risk. At the high end of the submassive risk spectrum are patients with abnormal biomarkers, such as a positive troponin and brain natriuretic peptide and evidence of RV dysfunction on CT or echocardiography. We would typically offer these patients Acoustic Pulse Thrombolysis™ therapy. In some institutions, patients with submassive PE are treated with anticoagulation, and for those patients who are at the lower-risk end of the spectrum, that may be reasonable. However, submassive PE is not a benign disease process, and it carries a 3-month mortality risk that can range as high as 25%.³ We have compelling data from the ULTIMA,⁴ SEATTLE II, and now OPTALYSE PE trials indicating that Acoustic Pulse Thrombolysis™ therapy, administered with the EKOS® device, rapidly and safely reverses RV dysfunction, which, in effect, moves an intermediate-to-high-risk patient for cardiovascular complications into the low-risk end of the spectrum. This cannot be done rapidly with anticoagulation alone, as the ULTIMA study showed.

Most of the referrals our team receives for PE management come from a mix of hospitalists, emergency

room physicians, and pulmonary/critical care physicians. Having options for lower tPA dosing and shorter duration has opened the door for new treatment alternatives in a subset of patients that we probably would not have considered before we had the OPTALYSE PE data. When we talk to patients, their response has been uniform, both within the trial and in practice. They are excited to hear that there is an option for lower-dose, shorter-duration therapy than what we had to offer in the past. At our institution, we are pleased to be able to offer an effective treatment that improves patient safety and comfort.

SUMMARY

OPTALYSE PE demonstrated that EKOS® therapy can rapidly reverse RV dysfunction with safe, low doses of a thrombolytic agent during a short duration of infusion time. Offering more advanced treatments, such as EKOS® therapy, has become the standard for how we treat our submassive PE patients after appropriate risk stratification. ■

1. Tapson VF, Piazza G, Goldhaber SZ, et al. Optimum duration and dose of r-tPA with the acoustic pulse thrombolysis procedure for submassive pulmonary embolism. Presented at: the American Thoracic Society International Conference; May 19–24, 2017; Washington, DC.

2. Piazza G, Hohlfelder B, Jaff MR, et al. A prospective, single-arm, multicenter trial of ultrasound-facilitated, catheter-directed, low-dose fibrinolysis for acute massive and submassive pulmonary embolism: the SEATTLE II study. *JACC Cardiovasc Interv.* 2015;8:1382–1392.

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4. Kucher N, Boekstegers P, Müller OJ, et al. Randomized, controlled trial of ultrasound-assisted catheter-directed thrombolysis for acute intermediate-risk pulmonary embolism. *Circulation.* 2014;129:479–486.

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OPTALYSE PE: EKOS® Offers New Options for Treating Submassive PE Patients

BY ANDREW S.P. SHARP, MBChB, MD, FRCP



Each year, approximately 48,000 people suffer from a pulmonary embolism (PE) in the United Kingdom. About 40% of these patients have submassive PE, a condition that presents a clinical challenge. The approved treatments for PE

in the United Kingdom are simple and include extreme blood thinning. Funding is limited for interventional treatments, so very few patients with submassive PEs receive them, meaning we are much further behind the curve on the adoption of these interventional therapies for treating submassive PEs. However, the results of OPTALYSE PE represent an important step toward obtaining more funding for the use of this technology in the United Kingdom and other European countries. This will allow us to offer safer, more efficient treatment of submassive PE.

LESSONS FROM THE PEITHO STUDY

In the United Kingdom, patients with submassive PE (or intermediate-risk PE) typically receive standard anticoagulation therapy. However, this can take up to 2 weeks for the body to adequately lyse the clot and resolve strain on the right side of the heart, leaving patients prone to decompensation into right-heart failure and shock, with low blood pressure, organ failure, and even death, as demonstrated in the PEITHO (Pulmonary Embolism Thrombolysis) study.¹

Although more aggressive treatment with systemic full-dose thrombolysis effectively dissolves the pulmonary clot and relieves strain on the right side of the heart, it is associated with high rates of bleeding. PEITHO demonstrated that treating submassive PE patients with full-dose, systemic thrombolysis leads to serious bleeding complications in 11.5% of patients (among patients > 75 years old, this risk is substantially higher). Essentially, PEITHO showed that every submassive/intermediate-risk patient saved with full-dose systemic thrombolysis was counterbalanced by another who suffered a life-threatening bleeding complication, including a 2% rate of intracranial hemorrhage.

THE GROWING EVIDENCE FROM ACOUSTIC PULSE THROMBOLYSIS™ THERAPY

With approximately 1,000 submassive PE patients per year suffering cardiovascular collapse or death in the

United Kingdom, we need more effective treatment options for this large proportion of patients. Presently, very few patients (numbering in the low hundreds each year) in the United Kingdom with either submassive or massive PE are receiving interventional treatments. The results of the OPTALYSE PE trial² add to a growing body of research suggesting that Acoustic Pulse Thrombolysis™ (BTG International) therapy using the EKOS® device (BTG International) relieves strain on the right side of the heart in a manner that is faster than with heparin alone and safer than with systemic thrombolysis.

OPTALYSE PE builds on the findings of two earlier studies of Acoustic Pulse Thrombolysis™ therapy, suggesting that treatment with the EKOS® device could be a safer and more efficient treatment for submassive PE than either anticoagulation or full-dose systemic thrombolysis. The ULTIMA study showed, in a prospectively powered randomized trial, that Acoustic Pulse Thrombolysis™, with an average tissue plasminogen activator (tPA) dose of 20 mg, more effectively relieved right-heart strain than heparin alone, with few serious bleeding complications.³

SEATTLE II⁴ provided further data that right-heart strain can be successfully relieved in the first 48 hours in patients with submassive PE using a standardized 24 mg of tPA for bilateral EKOS® devices (a 76% reduction in tPA dose compared with traditional thrombolytic therapy). OPTALYSE PE assessed several lower-dosing regimens, ranging from 8 to 24 mg for bilateral catheters (the significant majority of all cases). All regimens effectively reduced right-heart strain, with a similar reduction in CT-derived right ventricular/left ventricular diameter ratio at 48 hours of approximately 23% to 26% across all four treatment strategies assessed.

Across the three studies evaluating Acoustic Pulse Thrombolysis™ therapy for submassive PE, we now have a menu of doses and treatment durations for our patients. The question now is, which has the greatest net clinical benefit in this important group of patients?

IMPLEMENTING NEW PE TREATMENT STANDARDS

As Chief Investigator for OPTALYSE-UK, recruiting in up to 15 sites in the United Kingdom, we will examine

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this question while building further experience and support for the use of this therapy in a country where catheter-directed treatments are less frequently used than in the United States. As a Co-Investigator in the first OPTALYSE PE study, I have already begun incorporating the findings of OPTALYSE PE into my practice. Generally, I calibrate the tPA dose when using EKOS® therapy according to patient stability, degree of right-heart strain, clot burden, and bleeding risk. For example, in older patients with a relatively high bleeding risk due to comorbidities, I may opt for the lower doses used in OPTALYSE PE to reduce right-heart strain while minimizing bleeding risk. For a younger patient with a large volume of PE and significant right-heart strain, I will consider one of the higher doses used in OPTALYSE PE to dissolve more of the clot and further reduce residual thrombus burden.

CONCLUSION

There are 100 million cases of PE and other forms of venous thromboembolism worldwide each year.⁵ I believe that as we start to deliver these interventional treatments with lower and lower doses of thrombolytic agents, they will be understood to be safer and more

effective than current approaches. The United States is increasingly adopting Acoustic Pulse Thrombolysis™ into routine care, and I am hopeful that the United Kingdom will follow as we further build the evidence base. ■

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2. Tapson VF, Piazza G, Goldhaber SZ, et al. Optimum duration and dose of r-tPA with the acoustic pulse thrombolysis procedure for submassive pulmonary embolism. Abstract presented at: American Thoracic Society International Conference 2017; May 19–24, 2017; Washington, DC.
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5. The Lancet Haematology. Thromboembolism: an under appreciated cause of death. *Lancet Haematol*. 2015;2:e393.

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EKOS[®] Therapy Restores Quality of Life in Patients With Postthrombotic Syndrome

BY MARK J. GARCIA, MD, FSIR, FACR



For decades, physicians have advised their patients with chronic deep vein thrombosis (DVT) that they must simply live with the leg pain, edema, ulceration, and the often-devastating disability of postthrombotic syndrome (PTS). Aside from conservative management with anticoagulation and compression, there was little else to offer patients with PTS.

The recent ACCESS PTS study, sponsored by BTG International, has challenged that mindset. We can now offer millions of patients with PTS the chance to restore their quality of life (QOL) with endovascular treatment. Our multicenter, prospective, single-arm study—the first infrainguinal chronic DVT intervention trial—demonstrated that chronic DVT and PTS can be safely and effectively treated by recanalizing occluded veins with Acoustic Pulse Thrombolysis[™] therapy (BTG International) with balloon dilatation.¹ The 73 participants (77 limbs) had ultrasound-confirmed femoral DVT for a minimum of 6 months, had failed 3 months of conservative therapy, and continued to have PTS sequelae with a Villalta score of ≥ 8 . All patients received enoxaparin (1 mg/kg twice daily) for 48 hours before endovascular recanalization and up to 90 days after EKOS[®] treatment (BTG International). Patients underwent balloon dilatation of the occlusive DVT segments, followed by EKOS[®] therapy for a minimum of 12 hours. The mean duration of EKOS[®] therapy was 23 hours with a total tissue plasminogen activator (tPA) dose of 18.5 mg.

The study met its primary efficacy endpoint of a minimum of 50% of patients having at least a 4-point improvement in Villalta score at 30 days ($P = .003$). The total mean Villalta score improved by 6.1 points (35.5%) from baseline, and there was a 3.9-point improvement (27.6%) from baseline in mean venous clinical severity scores (VCSS) ($P \leq .0001$ for each). Patients' VEINES-QOL score also improved 21% from baseline at 30 days ($P \leq .0001$). One major bleed (epistaxis with severe complications) and one pulmonary embolism occurred within 30 days after treatment, which met the study's safety endpoint. In addition, the outcomes of the endovascular intervention at 180 days continue to look promising, and the study will continue to follow patients for 1 year.

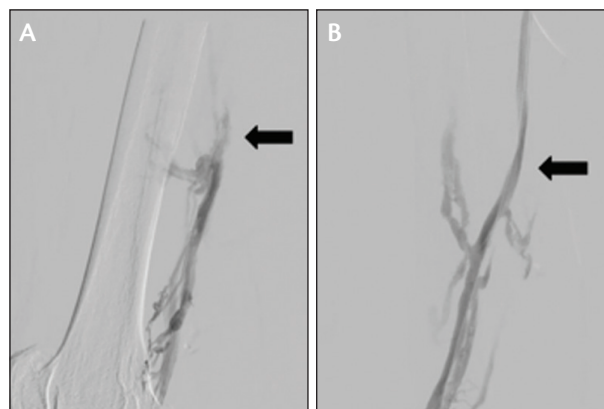


Figure 1. A 75-year-old woman presented with DVT of her right leg since February 2010 (> 5 years). Her baseline Villalta score was 15, which improved to 7 at 30-day follow-up. Pretreatment occlusion of the femoral vein (A). After percutaneous transluminal angioplasty and EKOS[®] treatment, the femoral vein was recanalized (B).

SIGNIFICANT SYMPTOM RELIEF

The endovascular approach used to treat PTS patients in ACCESS PTS, consisting of EKOS[®] therapy with balloon dilatation and adjunct therapy (if needed), significantly improved the patients' symptoms. However, the procedure takes time, patience, and perseverance to work through chronic occlusions and, in some ways, can be more challenging than an arterial chronic total occlusion case. Case examples of patients with DVT treated with EKOS[®] therapy are shown in Figures 1 and 2. We've found the following strategies to be helpful in achieving excellent outcomes.

A day or two before the procedure, we start patients on the anticoagulant enoxaparin (twice-daily dosing) to help prevent an acute thrombosis from occurring.

The success of the procedure depends on the operator establishing direct in-line flow from the patient's ankle to the heart. To best accomplish this, access into the vessel must be below the lowest level of disease, which I believe helps minimize rethrombosis. This most commonly entails accessing the posterior or anterior tibial veins at the ankle for the initial full-leg venogram and subsequent treatment techniques.

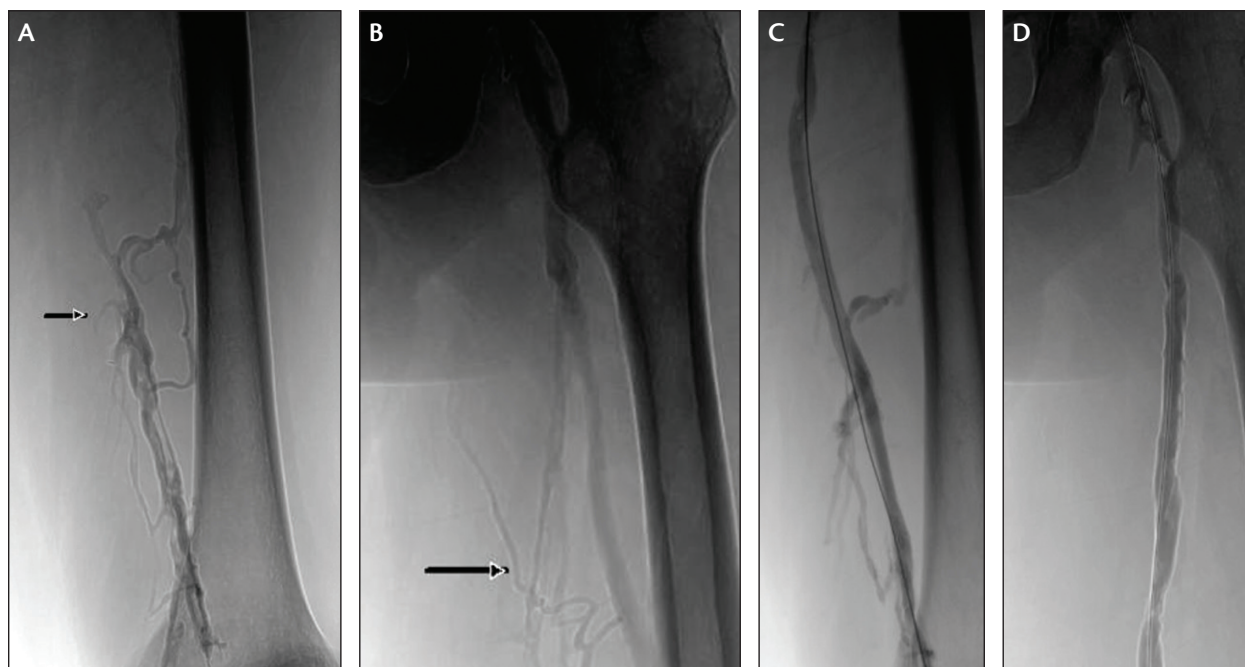


Figure 2. A 67-year-old man with a history of multiple episodes of DVT in 2006, 2007, and 2013. An inferior vena cava filter was placed in 2007 after DVT while on anticoagulation; he was diagnosed with prothrombin 20210 mutation and placed on lifelong warfarin. In November 2013, he developed DVT in both lower extremities and a large bilateral pulmonary embolism after discontinuing warfarin earlier in the month. The patient underwent DVT lysis of the inferior vena cava and both lower extremities, but there was no change in the extensive right lower extremity chronic DVT. In July 2014, he presented for evaluation of severe right lower extremity PTS and was enrolled in the ACCESS PTS trial. At baseline, the patient was CEAP 4b, with a Villalta score of 20 and a VCSS of 15. The initial pretreatment venogram showed chronic scarring and venous change of the popliteal artery with femoral vein occlusion (A, B). Posttreatment venograms showed recanalization with direct in-line flow from the popliteal artery through femoral veins (C, D). At 1 month posttreatment, the patient was CEAP 4b with a Villalta score of 4 and VCSS of 4. At 3-months posttreatment, the patient had improved to CEAP 2 with a Villalta score of 2 and VCSS of 5, and at 6 months, he was CEAP 2 with a Villalta score of 3 and VCSS of 5.

To cross the occlusion, I start by using the NaviCross device (Terumo Interventional Systems) and a stiff straight Glidewire (Terumo Interventional Systems), and if needed, I'll use the TriForce device (Cook Medical). When the venous occlusions are successfully crossed, a space is created with serial balloon venoplasty to the expected size of the "normal" vessel at that level. For example, I typically dilate the femoral vein up to 10 mm and the popliteal to 6 to 7 mm. It is important not to undersize these vessels during final balloon dilatation and to dilate in a slow and prolonged fashion to "stretch" the diseased vessel and help prevent recoil.

The early ACCESS PTS study results demonstrate that the ultrasound effect of EKOS® therapy is very effective. I believe that ultrasound helps soften the scarred vein walls and allows for better dilatation and remodeling, which may improve the vein wall compliance and function in the long run.

Our patients continue on enoxaparin for 1 month after the procedure, and then they transition to an oral anticoagulant, typically for a minimum of 1 year. Every patient I treat is also educated on the ABCs of self-care: activity, blood thinners, and compression.

CONCLUSION

Acoustic Pulse Thrombolysis™ with balloon dilatation should be considered in the appropriate setting for any patient with chronic DVT and PTS who does not have a contraindication to lytic therapy and who has failed conservative treatment. The results of the ACCESS PTS trial offer hope to patients with PTS. ■

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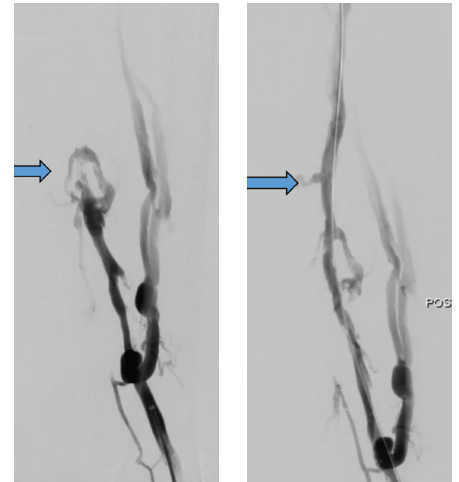
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Disclosures: Lead Investigator of ACCESS PTS; consultant and speakers bureau for Boston Scientific Corporation, Philips Volcano, and Ekos Corporation, a BTG International group company; research support from Boston Scientific Corporation and Ekos Corporation, a BTG International group company.



TREAT CHRONIC DVT AND PTS WITH THE ONLY PROVEN TREATMENT REGIMEN

- LEARN THE ACCESS PTS TECHNIQUE
FEATURING EKOS® THERAPY
- UNDERSTAND TIPS AND TRICKS FOR
CROSSING THE OCCLUSION
- REVIEW CHALLENGING CASES TO HELP
YOU PLAN AND EXECUTE CHRONIC DVT
TREATMENTS



Before ACCESS PTS
Villalta Score: 15

After ACCESS PTS
Villalta Score: 7*

* At 30 days



Featuring Mark J. Garcia, MD, MS, FSIR, FACR

Vascular & Interventional Associates of Delaware, LLC
St Francis Healthcare, Dept of VIR
Wilmington, Delaware

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FDA CLEARED INDICATIONS: The EkoSonic® Endovascular System is indicated for the ultrasound-facilitated, controlled, and selective infusion of physician-specified fluids, including thrombolytics, into the vasculature for the treatment of pulmonary embolism; the controlled and selective infusion of physician-specified fluids, including thrombolytics, into the peripheral vasculature; and the infusion of solutions into the pulmonary arteries. Instructions for use, including warnings, precautions, potential complications, and contraindications can be found at www.ekosc corp.com. Caution: Federal (USA) law restricts these devices to sale by or on the order of a physician.





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Bilateral PE treatment just got better.^{1,2,3,4}

Get the same EKOS[®] efficacy in 1/2 the time or less, with 1/2 the dose or less. The 2017 OPTALYSE PE randomized, multi-center study showed EKOS[®] two, four and six-hour treatments all relieved right heart strain, with efficacy similar to EKOS[®] current 12/24-hour treatment and r-tPA doses as low as 4 mg per catheter.^{1,4} Shorter treatments give physicians same-day scheduling options and lower doses enhance safety.¹ Visit www.ekosc corp.com to learn more about the only endovascular device cleared by the FDA for the treatment of pulmonary embolism.

EKOS[®] — Setting the standard in PE treatment.

- ¹ Tapson, et al, "Optimum Duration and Dose of r-tPA with the Acoustic Pulse Thrombolysis Procedure for Submassive Pulmonary Embolism: OPTALYSE PE," American Thoracic Society (ATS) Meeting, Washington, DC, May 2017.
- ² Lin, P., et al., "Comparison of Percutaneous Ultrasound-Accelerated Thrombolysis versus Catheter-Directed Thrombolysis in Patients with Acute Massive Pulmonary Embolism." *Vascular*, Vol. 17, Suppl. 3, 2009, S137-S147.
- ³ Nykamp M., et al. "Safety and efficacy of ultrasound-accelerated catheter-directed lytic therapy in acute pulmonary embolism with and without hemodynamic instability." *J Vascular Surgery: Venous and Lymphatic Disorders* 2015; 3(5): 251-7.
- ⁴ Piazza, G., et al., A Prospective, Single-Arm, Multicenter Trial of Ultrasound-Facilitated, Low-Dose Fibrinolysis for Acute Massive and Submassive Pulmonary Embolism: the Seattle II study." *Journal of the American College of Cardiology: Cardiovascular Interventions* 2015; 8: 1382-92.

FDA CLEARED INDICATIONS: The EkoSonic[®] Endovascular System is indicated for the ultrasound-facilitated, controlled, and selective infusion of physician-specified fluids, including thrombolytics, into the vasculature for the treatment of pulmonary embolism; the controlled and selective infusion of physician-specified fluids, including thrombolytics, into the peripheral vasculature; and the infusion of solutions into the pulmonary arteries. Instructions for use, including warnings, precautions, potential complications, and contraindications can be found at www.ekosc corp.com. Caution: Federal (USA) law restricts these devices to sale by or on the order of a physician. **THE CE MARK (CE0086) HAS BEEN AFFIXED TO THE EKOSONIC[®] PRODUCT WITH THE FOLLOWING INDICATIONS: Peripheral Vasculature:** The EkoSonic[®] Endovascular Device, consisting of the Intelligent Drug Delivery Catheter (IDDC) and the MicroSonic[™] Device (MSD), is intended for controlled and selective infusion of physician-specified fluids, including thrombolytics, into the peripheral vasculature. All therapeutic agents utilized with the EkoSonic[®] Endovascular System should be fully prepared and used according to the instruction for use of the specific therapeutic agent. **Pulmonary Embolism:** The EKOS EkoSonic[®] Endovascular System is intended for the treatment of pulmonary embolism patients with $\geq 50\%$ clot burden in one or both main pulmonary arteries or lobar pulmonary arteries, and evidence of right heart dysfunction based on right heart pressures (mean pulmonary artery pressure ≥ 25 mmHg) or echocardiographic evaluation.



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