Example of a PE protocol roadmap - use of a roadmap offers an effective and efficient care continuum for acute PE.

Pulmonary Embolism (PE) Protocol Roadmap:

1. PE symptoms are recognized
2. Go to ER
3. Call the local emergency service (EMS)
4. EMS assess
5. EMS identifies PE
6. EMS departs for the hospital
7. Go to ER

Settings:
- Community Hospital
- Primary PE center
- Comprehensive PE center
High risk RV function (echo or CT) laboratory testing
Assess clinical risk (PESI or sPESI)
Shock / Hypotension?
Yes
Diag nostic algorithm for suspected high-risk PE
Intermediate-low risk
Intermediate-high risk
Massive
Sub-massive
Minor
Low risk
Primary reperfusion
A/C; monitoring consider rescue reperfusion
A/C; hospitalization
A/C; consider early discharge & home treatment, if feasible
No
Intermediate risk
PE Confirmed
Consider further risk stratification
Diagnostic algorithm for suspected not high-risk PE
PE Confirmed
Assess clinical risk (PESI or sPESI)
PESI Class III-IV or sPESI ≥ 1
PESI Class I-II or sPESI = 0
RV function (echo or CT) laboratory testing
Both positive
One positive or both negative
High risk
Intermediate-high risk
Intermediate-low risk
Low risk
Primary reperfusion
A/C; monitoring consider rescue reperfusion
A/C; hospitalization
A/C; consider early discharge & home treatment, if feasible

† ESC Guidelines on the diagnosis and management of acute pulmonary embolism. European Heart Journal. doi:10.1093
EKOS Corporation, a BTG International group company, is committed to advancing the treatment of acute pulmonary embolism (PE). Through technological innovation, such as Acoustic Pulse Thrombolysis™ treatment, and a comprehensive approach to clinical research, EKOS® is dedicated to improving patient outcomes. Our approach, however, extends beyond devices – our goal is to be your ally in improving the patient treatment pathway, from onset to recovery. The EKOS® team and our distribution partners are at your disposal to provide – and help implement – a series of programs to help your facility treat PE patients more safely and effectively.

Pulmonary Embolism ALERT
Think Fast, Act Together!™
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What is Acute Pulmonary Embolism (PE)?

PE is a condition where one or more clots break off and travel from existing venous clots in the arms or legs in the circulatory system, getting trapped in the pulmonary arteries, where they can block blood flow and access to the lungs’ vital oxygenation system. In intermediate-risk or high-risk cases, this may lead to a strain on the heart’s ability to pump blood through the lungs which can then lead to heart failure and/or cardiovascular collapse.

Common PE symptoms include:
- Shortness of breath
- Progressively worsening chest pain
- Cough
- Clammy or discoloured skin
- Excessive sweating
- Rapid or irregular heartbeat
- Lightheadedness or dizziness

PEs can be immediately fatal. However, if PE can be diagnosed and appropriate therapy started, the mortality can be reduced from approximately 30 percent to less than 10 percent.  

Public Awareness

Annual incidence
- Over 600,000 cases annually in the US²
- Responsible for more deaths in the EU each year than breast cancer and AIDS combined³,⁴
- PE causes or contributes to 15% of all hospital deaths⁵,⁶

Venous thromboembolism¹
- PE commonly originates from lower limb deep vein thrombosis (DVT)
- 79% of patients presenting with PE have evidence of DVT
- PE occurs in up to 50% of patients with proximal DVT
Emergency Medical Services and Emergency Department

PE Alert Checklist
Pre-hospital identification is a vital initial step in the emergency medical management of PE. A symptoms-based screening tool facilitates rapid, standardized, symptomatic clinical assessment. Based on the assessment, routing the acute PE patient to the most appropriate treatment facility which offers the latest therapies and interventional technologies, including the EKOS® system, will improve outcomes for patients.

Emergency Department
When someone suffers an acute PE, recognizing symptoms, calling 911, response by EMS, and transportation to the Emergency Department with diagnostic and treatment capabilities can make a significant impact on a successful outcome.

Rapid assessment, knowing what level of PE care each hospital offers and whom to contact within the hospital are critical to optimizing an acute PE patient’s outcome. Developing an acute PE network, with incorporation of a PE Response Team (PERT) and implementation of a standardized critical care pathway is an innovative and effective treatment approach for acute PE.8

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79% of patients presenting with PE have evidence of DVT

PE occurs in up to 50% of patients with proximal DVT
Specialties Involved in the PE Patient Pathway

ICU/CCU:
Before and after placement of the EKOS® Device, a patient with PE (risk stratification: intermediate-high and high) is admitted to the Intensive Care Unit (ICU).

Interventional Radiologists, Interventional Cardiologists, and Vascular Surgeons:
Placement of the EKOS® Device is usually done by an Interventional Radiologist, Interventional Cardiologist, or a Vascular Surgeon and their team. The procedure is carried out in the cath lab or angio lab under fluoroscopy. They use catheters and wires to navigate through the vasculature and usually place the EKOS® Device in the lower branch of the pulmonary artery.

Vascular Medicine:
In some hospitals, Vascular Surgeons play a key role in the treatment of PE because of their diagnosis and treatment of DVT. A high number of PE patients have had a DVT. In many hospitals, Vascular Surgeons are part of the PERT program and place the EKOS® Device in PE patients.

Internal Medicine, Vascular Medicine, and Pulmonologists:
Assessment of the status of a PE patient and decision on treatment is a multidisciplinary approach where other groups play a key role as well. Depending on the patient situation at onset, i.e. coming into the Emergency Department or already admitted to the hospital because of comorbidities, several doctors are included in the decision-making process.

To facilitate an easier decision-making process, a PERT approach has been shown to be beneficial to the patient. In this way, protocols have been prepared and discussed prior to the arrival of an acute PE patient.

Other Specialties:
Orthopedists, Hematologists, and Oncologists can see patients who develop a PE due to the patient disease. They refer patients to the ICU or the PERT.

Administrators and Executives:
Caring for patients suffering from PE takes a concerted effort of many medical specialties and technologies to optimize patient care. In order to have a successful PERT, the executive board must consider the following:

• Manpower
• Imaging and angiography equipment
• Intensive care unit
• Raising awareness for the new PERT program in the community

Building a comprehensive PE program center should be a collaborative effort involving the physicians, and should include measures of quality, resource utilization, efficiency, and market development. Benefits of committing to a PERT program include the ability to better serve the community and bring more patients into the institution.
Circle Strategy
PE Referral Center and PE Response Team (PERT)

* Interventional cardiologist, interventional radiologist or vascular surgeon.
The EKOS® system includes an Ultrasonic Core within an Infusion Catheter and the Control Unit.

**Targeting the Thrombus, Safely**

With EKOS® Acoustic Pulse Thrombolysis™ treatment, most of the drug remains in the thrombus and typically, less lytic is used. It dissolves the thrombus, without damaging vessels, valves or walls.\(^9,10\) There is no mechanical disruption resulting in distal embolization.\(^1,1\)

The EKOS® system’s safety and efficacy is supported by Level 1 and Level 2 data.\(^1,12,13,14,15\)

**Reduced Procedure Time**\(^16,17\)

EKOS® requires significantly shorter treatment times, typically only 33–50% of standard CDT. Unlike more complex surgical solutions,\(^18,19\) EKOS® is an efficient, three-step process:

1) Insert the EKOS® 5.4 F Infusion Catheter through the thrombus.

2) Insert the ultrasonic core and luer lock into place.

3) Activate the lytic infusion and begin Acoustic Pulse Thrombolysis™ treatment.
Treatment zones range from 6cm to 50cm with radiopaque marker bands at each end of the treatment zone to enhance visualization. At-a-glance operating status, alarms and treatment times are easy to read from a distance.

EKOS® Acoustic Pulse Thrombolysis™ treatment is a minimally invasive system for dissolving thrombus. The Ultrasonic Core generates a localized acoustic field which greatly accelerates lytic dispersion by driving the drug deeper into the clot and unwinding the fibrin strands to expose plasminogen receptor sites.

Acoustic Pulse Thrombolysis™ Treatment:
• Speeds time-to-dissolution
• Increases thrombus removal and clinical improvement compared to either standard Catheter Directed Therapy (CDT) or thrombectomy18,19
• Lowers the risk of bleeding and other complications17,18

More Effective Drug Delivery:
• Reduces dosage requirements by as much as 68% compared to standard CDT17
• Requires up to 4x less drug dosage than systemic delivery12,13

Superior Thrombus Clearance16,17:
• 48% greater drug absorption within 1 hour20
• 84% greater drug absorption within 2 hours20

The Thrombosis Barrier
Tightly wound fibrin strands prevent lytic from reaching receptor sites

With Acoustic Pulse
Ultrasonic energy thins fibrin strands and exposes receptor sites

With Acoustic Pulse + Lytic
More drug reaches entire thrombus, accelerating absorption
Randomized, Controlled Trial of Ultrasound-Assisted Catheter-Directed Thrombolysis for Acute Intermediate-Risk Pulmonary Embolism

*Nils Kucher, MD et al. Circulation 2014; 129: 479-486*

**Patients**

**Acute PE with RV/LV ratio ≥ 1.0**

**Methods**

**Infusion Protocol**

- rtPA 1mg/h; saline coolant 35ml/h
- Patients monitored in the intermediate or ICU
- After five hours, rtPA reduced to 0.5mg/h
- At 15 (+/- 1) hours, rtPA infusion, saline coolant and ultrasound discontinued
- Removed in the intermediate or ICU

**Unfractionated heparin + Ultrasound-assisted CDT using EKOS®**

**Unfractionated heparin**

Unfractionated heparin administered immediately after randomization
The ULTIMA Trial
Key Results & Conclusion

**Conclusion:** ULTIMA confirmed that a fixed-dose, ultrasound-assisted catheter-directed thrombolysis using EKOS® regimen was superior to anticoagulation alone in improving RV dysfunction at 24 hours without an increase in bleeding complications.
A Prospective, Single-Arm, Multicenter Trial of Ultrasound-Facilitated, Low-Dose Fibrinolysis for Acute Massive and Submassive Pulmonary Embolism


Patients
Acute Massive and Submassive PE with RV/LV ratio \( \geq 0.9 \) (\( n = 150; 22 \) centers)

Methods
Ultrasound-facilitated fibrinolysis using EKOS®

If unilateral PE:
- tPA 1 mg/hr using one EKOS® system for 24 hours

If bilateral PE:
- tPA 1 mg/hr/per EKOS® system (using two simultaneously) for 12 hours

Follow up at 48 +/- 6 hours
- CT measurement of RV/LV ratio
- Echocardiogram to estimate PA systolic pressure
Conclusion: Ultrasound-facilitated, catheter-directed, low-dose fibrinolysis for acute PE improves RV function and decreases pulmonary hypertension and angiographic obstruction. By minimizing the risk of intracranial bleed, it represents a potential “game-changer” in the treatment of high-risk PE patients.
EKOS® PE Clinical Studies

Ultrasound-Accelerated Catheter-Directed Thrombolysis for Acute Submassive Pulmonary Embolism.

*J Vasc Interv Radiol* 2015; 26(7): 1001-1006

**A single-center, retrospective study**
*(15 patients enrolled prospectively in SEATTLE II)*

**Authors/Investigators:**
Sandeep Bagla, MD, John B. Smimioutopoulos, MD, Arletta van Breda, MSN, Michael J. Sheridan, ScD, and Keith M. Sterling, MD from the Cardiovascular and Interventional Radiology department at Inova Alexandria Hospital in Alexandria, VA, USA

**Objective:**
To evaluate the safety and efficacy of EKOS® treatment in patients with submassive PE.

**Results:**
EKOS® treatment was technically successful in all 45 (100%) patients.

- A statistically significant decrease in PA pressure from an average of 49.8 mmHg to an average of 31.1 mmHg (p<.0001)
- There was complete concordance between PA pressures measured via the EKOS® catheter and the angiographic catheter in three patients who underwent measurements both ways
- A statistically significant decrease in RV:LV ratio from an average of 1.59 to 0.93 (p<.0001)
- No patient died through the 30-day follow up, and there were no 30-day readmissions for PE
- Four minor bleeding episodes at access sites
- Two major bleeding episodes – one patient had flank hematoma 3 days post-lysis possibly due to supratherapeutic anticoagulation, and one patient had major bleeding from a previous brachial artery blood-gas puncture site
A single-center retrospective review of 45 (26 men and 19 women) patients undergoing EKOS® treatment for acute massive or submassive PE between Jan 2011 – Dec 2013

Authors:
Madeline Nykamp, Angela VandenHull, Tyler Remund PhD, Angelo Santos MD, Patrick Kelly MD, Greg Schultz MD, and Chad Laurich MD, of Sanford Vascular Associates in Sioux Falls, SD, USA

Objective:
To evaluate the safety and effectiveness of ultrasound-accelerated thrombolysis in acute pulmonary embolism.

- Patients had either massive PE as evidenced by hemodynamic instability (defined as systolic bp <100 mm Hg; tachycardia >100 beats/min), or submassive PE defined as:
  - right-heart strain evidenced by RV dilation, septal deviation, or hypokinesis
  - right ventricle dilatation by CT scan or
  - pulmonary hypertension by direct catheter measurement
- A separate “control group” of 45 intermediate to massive PE patients who were treated with systemic infusion of heparin or anticoagulation from 2011 to 2013 were randomly selected. Their charts were reviewed for similar demographic and baseline characteristics, periprocedural parameters, and follow-up information. This allowed for comparison of EKOS® treatment vs. heparin

Results:
- The average length of hospital stay for the EKOS®-treated group was 3.2 days (± 2 SD), which was significantly shorter when compared to 6.7 days (± 4.4 SD) for the anti-coagulation control group
- Survival in the EKOS® treated group when followed up to 2 years was significantly higher compared to the anti-coagulation control group
- No deaths through 90 days of follow-up and no major periprocedural bleeding events
- EKOS® treated patients received a total average rtPA dose of 30.5 mg (range 14-66 mg) over 14.2 hours (range, 8-21 hrs). However, over two-thirds (31) of patients did not receive a bolus of rtPA and received a total dose of 22.5 mg rtPA (range, 14-48 mg)
Circle Strategy Programs

Annual Regional Network Meeting

Objective:
Circle Strategy Programs are held to strengthen the relationship between the different teams in the Pulmonary Embolism care chain of your hospital. The development of regional networks that link primary care hospitals and physicians to comprehensive pulmonary embolism centers can help to improve patient outcomes.

Suggested topics to cover:
• Patient flow and transfers from referring hospitals
• What is required from referring hospitals?
• Protocol discussion
• Endovascular treatment of pulmonary embolism
• Patient selection
• Intensive care
• Case discussions
• Management of complications
• Latest clinical data

Please contact your EKOS® Representative for more information.

PE Center of Excellence Training

Duration: 1 day
Sites: Coming Soon

Objective:
• Educate interventionalists and other specialties on acute pulmonary embolism treatment and considerations
• Develop/modify PE protocols – patient selection and diagnostics
• Workshop includes didactic presentations and review of clinical experience

This workshop is dedicated to teams of interventionalists and other specialties from the same hospital who want to initiate a PERT program in their center.

Please contact your EKOS® Representative for more information.
EKOS® User Meetings

Regional Pulmonary Embolism Updates

Objective:
EKOS® Users Meetings are held regionally throughout the year to educate your team of interventionalists, ER staff, Cath Lab staff, ICU nurses and other specialties. The intent of the User Meetings is to learn from world renowned faculty who engage in a comprehensive approach to the treatment of Pulmonary Embolism – from symptom onset to recovery. Our esteemed faculty will identify rapid assessment, diagnosis, imaging, and treatment options from lytics and best-medical management, to best-practices around the use of the EKOS® system and Acoustic Pulse Thrombolysis™ therapy.

Suggested topics to cover:
• Patient flow and transfers from referring hospitals
• Imaging in pulmonary embolism
• Patient selection (guidelines and risk stratification)
• Intensive care
• Latest clinical data
• Management of complications
• Case discussion

Please contact your EKOS® Representative for more information.

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EKOS® Scientific Exchange

Duration: 2 days
Sites: Bothell, WA

Objective:
• Production tour and discuss a PERT organization in a US hospital
• Gain more insight into the PE protocol, patient selection, patient workflow, imaging, and networking with specialties and surrounding hospitals, etc.

This workshop is dedicated to hospitals that want to improve their PE care pathway.

Please contact your EKOS® Representative for more information.
EKOS is a growing international specialist healthcare company bringing to market innovative products in specialist areas of medicine to better serve doctors and their patients. We have a portfolio of Interventional Medicine products to advance the treatment of liver tumor, advanced emphysema, severe blood clots and varicose veins, and Specialty Pharmaceuticals that help patients overexposed to certain medications or toxins. Inspired by patient and physician needs, BTG is investing to expand its portfolio to address some of today’s most complex healthcare challenges.

To learn more about BTG, please visit: www.btgplc.com.

FDA CLEARED INDICATIONS: The EkoSonic® Endovascular System is intended for controlled and selective infusion of physician-specified fluids, including thrombolytics, into the peripheral vasculature. The EkoSonic® Endovascular System is intended for the infusion of solutions into the pulmonary arteries. 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.