A. Program Demographics
1. Name of Host Institution
   Carolinas Medical Center, Charlotte NC

2. Program Specialty/Subspecialty
   Emergency Medicine/Clinical Research

3. Program Address (Mailing)
   1000 Blythe Blvd
   Department of Emergency Medicine
   MEB 306A
   Carolinas Medical Center
   Charlotte, NC 28203

4. Program Address (Physical location, if different from mailing)
   See #3

5. Program Phone Number
   704 355 7092 (Priscilla)
   704 355 8155 (Kline)

6. Program Fax Number
   704 355 7047

7. Program E-mail
   jkline@carolinas.org

8. Program Director
   Jeffrey A. Kline MD

9. Alternate Program Contact

B. Introduction
1. History. Identify how long the program has been in existence and include the number of individuals who have completed the training program since its inception

First fellow trained in 1995 and eight fellows total trained. Please see Kline CV under “individuals formally mentored in research”

2. Duration. Define an exact duration for the training program.
   Minimum of one year with two years preferred.

3. Prerequisite Training/Selection Criteria. Identify prerequisite training requirements and other selection criteria used in appointing candidate(s).
   Minimum of an medical doctorate (MD) or equivalent training. Board certified or board eligible in emergency medicine preferred.
4. Goals and Objectives for Training. Define the educational purpose of the training program and intended goals of the training program.

To learn how to independently design, perform, fund, and generalize the findings of clinical research. Topics include venous thromboembolism and infection/sepsis. Methodology covers study design, human subjects, ethics, regulatory issues, grant applications, manuscript preparation and oral presentation. Study types include clinical studies of diagnosis, device development, and clinical trials.

5. Program Certifications. List any additional certifications or recognitions that the program may hold.

The associated residency in emergency medicine is accredited by the RRC.

C. Resources

1. Teaching Staff. List the teaching staff involved in providing the educational experience and their supervisory responsibilities over the participant(s). It is not necessary to send a faculty member’s Curriculum Vitae (C.V).

Jeffrey A. Kline MD—Faculty and program director
Alan E. Jones MD—Faculty and assistant program director
Alice M. Mitchell MD—Faculty and associate director
Jackeline Hernandez MD—project manager over all clinical studies
Melanie M. Hogg, MS—director of regulatory affairs and device development

2. Facilities. List all training sites where rotations are conducted.

Carolinas Medical Center, Main campus

D. Educational Program – Basic Curriculum

Describe the following elements of the training program.

1. Clinical and research components.

For ABEM-certified or eligible candidates, 12 clinical hours per week in the emergency department at Carolinas Medical Center.

Minimum research requirements include completion of one clinical study with associated manuscript accepted for publication in a peer reviewed journal. Completion and submission of one extramural grant application. Oral presentation of one abstract. Also expected to be or become proficient in document handling, spreadsheet management (Excel) and using a statistical software package (TBA).

2. Participant’s supervisory and patient care responsibilities.

8-12 clinical hours per week in the emergency department. Includes supervising residents from all services.

3. Procedural requirements.

Ability to stand and walk.

4. Didactic components.
• Weekly research meeting.
• Journal article reading as prescribed
• Completion of institutional and federal training modules (e.g., IRB required training to obtain informed consent)
• Reading of suggested books on biostatistics, elements of research design, the GCP/ICH manual, and the chosen topic.
• Optional attendance to the residency noon didactic sessions
• One hour per week with any of the faculty in a one-on-one discussion of research related topics.
• See attached syllabus for outline of statistical and methodology concepts to gain experience/expertise using.

5. If the program is more than twelve months in duration, please describe the progression in responsibilities by PGY level.

The second year will be contingent on progress in the first year. Most worthy clinical studies require at minimum, 18 months to design and execute. Candidates may opt to pick up ongoing studies which will require less time to complete, but will instill less independence.

E. Evaluation
Describe the formal evaluation process used to assess the educational performance of program participants.

Primarily verbal during regular meetings with the Program Director.
## Research Fellowship Learning Objectives.

<table>
<thead>
<tr>
<th>Objective</th>
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<tbody>
<tr>
<td>1. Identification of Area of Focus</td>
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<td>2. Hypothesis Generation</td>
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<td>3. Research Design</td>
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<td>3.1. Definition of Study Population or Model System</td>
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<td>3.2. Definition of Endpoints</td>
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<tr>
<td>3.2.1. Relevance</td>
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<td>3.2.2. Reliability</td>
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<td>3.2.3. Validity</td>
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<td>3.3. Interventions</td>
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<td>3.4. Sample Size Determination/Power Analysis</td>
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<td>3.5. Planned Comparisons and Analyses</td>
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<td>3.5.1. Primary Endpoint</td>
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<td>3.5.2. Multiple Endpoints vs. Composite Endpoints</td>
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<td>3.5.3. Subgroup Analyses</td>
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<td>3.5.4. Adjustment for Covariates</td>
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<td>3.5.5. Modeling</td>
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<tr>
<td>4. Data Collection Methods</td>
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<td>4.1. Data Collection Form and Case Report Form (CRF) Design</td>
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<td>4.2. Testing and Revision of Case Report Forms</td>
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<td>4.3. Database Design</td>
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<td>4.4. Data Verification and Query Resolution</td>
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<td>5. Data Monitoring and Interim Data Analysis</td>
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<td>5.1. Data Monitoring Committees</td>
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<td>5.2. Statistical Aspects of Interim Data Analysis/Efficacy Monitoring</td>
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<td>5.3. Safety Monitoring</td>
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<td>6. Data Analysis</td>
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<td>6.1. Verification of Data Quality</td>
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<td>6.2. Verification of Assumptions</td>
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<td>6.2.1. Quality of Randomization</td>
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<td>6.2.2. Characteristics of Study Population</td>
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<td>6.2.3. Sample Size Assumptions</td>
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<td>6.3. Data Analysis</td>
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<td>6.3.1. Primary Endpoints</td>
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<td>6.3.2. Secondary Endpoints</td>
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<td>6.3.3. Advanced Methods</td>
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<td>6.3.3.1. Multivariate Logistic Regression</td>
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<td>6.3.3.2. Classification and Regression Tree Analysis</td>
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<td>6.3.3.3. Decision Analysis</td>
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<td>6.3.3.4. Cost Analysis</td>
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<td>6.3.3.5. Bayesian Methods</td>
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<td>6.3.4. Exploratory Data Analysis</td>
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<td>6.3.4.1. Data-Motivated Analyses</td>
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### Research Fellowship Learning Objectives (continued).

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<td>Manuscript Preparation, Submission, and Revision</td>
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<td>Manuscript Outline</td>
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<td>Manuscript Revision and Interaction with Editors</td>
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<td>Responding to “Letters to the Editor”</td>
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<td>Grant Preparation, Submission, and Revision</td>
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<td>Project Management</td>
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<td>Personnel Management</td>
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<td>10.4.</td>
<td>Interaction with External Agencies</td>
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<td>11.</td>
<td>Ethical Aspects of Medical Research</td>
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<td>11.1.</td>
<td>Human Subject Protection</td>
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<td>11.2.</td>
<td>Use of Animal Subjects</td>
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<td>11.3.</td>
<td>Research Fraud and Misconduct</td>
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<td>12.</td>
<td>Informatics</td>
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<tr>
<td>12.1.</td>
<td>Personal Productivity Software</td>
</tr>
<tr>
<td>12.1.1.</td>
<td>Word Processing, Presentation Graphics</td>
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<tr>
<td>12.1.2.</td>
<td>Scientific Graphics</td>
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<td>12.1.3.</td>
<td>Personal Information Management</td>
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<tr>
<td>12.2.</td>
<td>Scientific Graphics</td>
</tr>
<tr>
<td>12.3.</td>
<td>Poster Creation</td>
</tr>
<tr>
<td>12.4.</td>
<td>Web Page Design</td>
</tr>
<tr>
<td>12.5.</td>
<td>Database Design and Translation</td>
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<td>12.6.</td>
<td>Statistical Software</td>
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<tr>
<td>13.</td>
<td>Teaching Skills</td>
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<tr>
<td>13.1.</td>
<td>Clinical Supervision</td>
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<td>13.2.</td>
<td>Lecture Preparation</td>
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<td>14.</td>
<td>Career Development</td>
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<td>Skill Development</td>
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<td>14.2.</td>
<td>Development and Maintenance of Collaboration and Mentor Relationships</td>
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<td>14.3.</td>
<td>Time Management</td>
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<td>14.4.</td>
<td>Requirements for Academic Promotion</td>
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</table>
CURRICULUM VITAE
JEFFREY A. KLINE, M.D.

Name: Jeffrey Allen Kline, MD
Work Address: Department of Emergency Medicine
1000 Blythe Blvd
MEB 306A
Charlotte, NC 28303
Phone: (Office) 704-355-7092
Date & Place of Birth: September 3, 1964 - Anchorage Alaska

Education:

Chief Resident - Emergency Medicine
Carolinas Medical Center
Charlotte, North Carolina  1993-1994

Research Fellowship - Emergency Medicine
Carolinas Medical Center

Residency - Emergency Medicine
Carolinas Medical Center
Charlotte, North Carolina  1990-1993

Doctor of Medicine
Medical College of Virginia
Richmond, Virginia  1986-1990

Bachelor of Science, Major: Biochemistry, Minor: English
Virginia Polytechnic Institute and State University
Blacksburg, Virginia  1982-1986

Professional Experience:

Director of Research  2001-present
Department of Emergency Medicine
Carolinas Medical Center

Assistant Director of Research  1995-2001
Department of Emergency Medicine
Carolinas Medical Center
Academic Faculty – 1994-Present
Department of Emergency Medicine
Carolinas Medical Center
Charlotte, North Carolina

**Academic Appointments**
Professor of Emergency Medicine
Department of Emergency Medicine
University of North Carolina School of Medicine
Chapel Hill NC  December 2007

Adjunct Faculty
Department of Biology
Queens University
Charlotte, NC  2006-present

Adjunct Professor
Department of Biology
Member, Graduate Faculty, Department of Biology
Faculty, Interdisciplinary PhD in Biology program
University of North Carolina, Charlotte
Charlotte NC  1999-present

**Hospital Appointments:**
Carolinas Medical Center
Department of Emergency Medicine
Assistant Director of Research
Charlotte, North Carolina  1994-Present

Assistant Professor of Emergency Medicine
University of North Carolina
Chapel Hill, North Carolina  1994-Present

**Certification/Licensure:**
North Carolina License #35398  1992-Present

**Airplane Ratings:**
ASEL/IFR  1990/1992

**Active Professional Societies:**
International Society for Thrombosis and Haemostasis  2003-Present
Fellow, American College of Emergency Physicians  2001-Present
Mecklenburg Medical Society  2000-2003
Shock Society  1995-2003
Society for Academic Emergency Medicine  1992-Present

**Community service**
Boy Scouts of America, Den/troop leader  2007-present

**SERVICE-NATIONAL ORGANIZATIONS**
American College of Emergency Physicians
Emergency Medicine Foundation
Emergency Medicine Research Fellowship

- Committee Chair 2006-2008
- Board of Trustees, Secretary-Treasurer 2005-2006
- Basic science study section chair 2004-present
- Board of Trustees 2004-2005
- Emergency Medicine Basic Research Seminar 2001-present
  - Institutional Review Board issues/ethics/research startup
- Scientific Review Committee 1999-present
- DVT/PE Subcommittee 1999-2002
- Chest Pain Subcommittee 1998-2002

American Society of Hematology
- Workshop on Thrombosis Surveillance 2008

American Heart Association
- AHA writing group "Venous Thromboembolic Disease: Management of Massive Pulmonary Embolism, Iliofemoral DVT, and Chronic Thromboembolic Pulmonary Hypertension." 2009

National Institutes of Health
- Medical-Surgical Emergency Care Research Roundtable 2009

Society for Academic Emergency Medicine (SAEM)
- Guidelines Committee 2007-2008
- Program Committee 2002-2004
  - Subcommittee chair: Scientific Subcommittee 2002-2004
- Research Committee 1995-2002
  - Subcommittee chair: Critical review of grants 2001-2002
  - Subcommittee chair: successful researchers project 2000-2001

Task Force appointments
- Research Fund 501C Task Force (Chair) 2007-2008
- Academic Faculty Development 1996-1997

ELECTED POSITIONS
- SAEM President Elect 2009
- SAEM Board of Directors, Secretary-Treasurer 2007-2009
  - Major projects/proposals
    - Intellectual property protection
    - Academic Emergency Medicine journal manager subgroup
    - Academic Emergency Medicine publishers task force
    - Creation of the Research Foundation
    - Chair, non-dues revenue enhancement task force
    - Chair, SAEM office relocation task force
  - Liaison Roles
    - Finance Committee 2007-present
    - Development Committee 2006-2007
    - Ultrasound Interest Group 2005-2007
    - Goal Directed Therapy Interest Group 2005-2006
    - Industry Relations Task Force 2005-2006
    - Research Committee 2004-2007
    - Research Committee 2008-2009
Emergency Medicine Research Fellowship

Grants Committee 2005-2007
Evidence Based Medicine Interest Group 2004-2007
SAEM BOD representative to the EMF BOT 2004-2007
SAEM Research Foundation Inaugural Secretary-Treasurer 2008
ACEP EMF Board of Trustees Secretary-Treasurer 2005-2009
SAEM Board of Directors 2004-2009
SAEM Nominations Committee 2001-2003

INSTITUTIONAL
CMC Council on Innovation 2008-present
Physicians Leadership Institute 2008
Research Advisory Committee 2008
Intellectual Property Committee 2008
Research Website Committee 2008
ScholarTrack™ Project Manager 2007-2008
Internal Medicine Chair Search Committee 2007
Body Worlds Planning Committee 2007
Institutional Review Board 1999-present
Animal Care and Use Committee 1996-1999
Research Review Committee 1994-1996

Honors/Awards

COLLEGE
• 1986-Most Outstanding Senior in Biochemistry
• 1986-Who's Who Among American Colleges and Universities
• 1986-Phi Beta Kappa
• 1985-Omicron Delta Kappa

MEDICAL SCHOOL
• 1989-Alpha Omega Alpha, Junior, Brown-Sequard Chapter
• 1989-Sydney Barham Scholarship for Academic Achievement

RESIDENCY
• 1994-Outstanding Resident Award
  Department of Emergency Medicine, Carolinas Medical Center,
• 1994-Outstanding Resident Research Award
  Department of Emergency Medicine, Carolinas Medical Center

FACULTY
• 2009-Excellence in Research Award, Society for Academic Emergency Medicine
• 2006-Best Oral Presentation Awards 1. Faculty (Alan Jones), 2. Fellow (Alice Mitchell), and 3. Medical Student (Brad Stevinson), SAEM Southeast Regional Meeting, Greensboro, NC.
• 2005-Best Faculty Poster “Use of expired CO2 and O2 to diagnose pulmonary embolism.” SAEM Southeast Regional Meeting, Chapel Hill.
• 2005- Best Oral Presentation (Alice Mitchell, presenter) “Novel protein markers for acute coronary syndrome” SAEM Southeast Regional Meeting, Chapel Hill.
• 2004-Best Clinical Science Presentation, Young Investigator (Alan Jones, presenter) “Randomized controlled trial of early versus delayed ultrasound for the diagnosis of undifferentiated hypotension in emergency department patients. SAEM Annual Meeting, Orlando, FL.
• 2004- Best Oral Presentation (Michael Runyon, presenter) “Unstructured physician estimate of low risk for pulmonary embolism is equivalent to the Canadian score and the Charlotte score” SAEM Southeast Regional Meeting, Chapel Hill.
• 2002-Best Oral Presentation “Use of Vital Signs to Risk-Stratify Emergency Department Patients with Pulmonary Embolism” SAEM Mid-Atlantic Meeting, Wilmington, DE.
• 2000-SAEM Young Investigator Award.
• 1999-Award for Excellence in Teaching Department of Emergency Medicine, Carolinas Medical Center, Resident Research Day.
• 1998-Best Oral Presentation “Use of volumetric capnography and neural analysis to diagnose pulmonary embolism” SAEM Mid Atlantic Regional Meeting, Charlottesville, VA.
• 1995-Established Investigator Award
  American College of Emergency Physicians $5,000.00

Publications:
Book Chapters:

Publications – Full-length, Peer Reviewed:
*Indicates role as senior author with responsibility for correspondence
IN PRESS
Burnside PB, Kline JA. Indirect Computed Tomography Venography: Quality of Vascular Opacification and Diagnostic Implications. Emergency Radiology
Watts JA, Gellar MA, Obraztsova M, Kline JA. Proinflammatory events in right ventricular damage during pulmonary embolism: Effects of treatment with ketorolac in rats. *J. Cardiovasc Pharmacol*

MR Marchick, JA Kline, AE Jones. Significance of non-sustained hypotension in emergency department patients with sepsis. *Intensive Care Medicine*

Kline JA, Steuerwald MT, Marchick MR, Hernandez J, Rose GA. Prospective evaluation of right ventricular function and functional status six months after acute submassive pulmonary embolism: Frequency of persistent or subsequent elevation in estimated pulmonary artery pressure. *Chest*

Zagorski J, Obraztsova M, Gellar MA, Kline JA, Watts JA. Transcriptional changes in right ventricular tissues are enriched in the outflow tract compared to the apex during chronic pulmonary embolism in rats. *Physiological Genomics*


In revision
Zagorski J, Marchick MR, **Kline JA**. Rapid clearance of circulating haptoglobin from plasma during acute pulmonary embolism in rats results in HMOX1 up-regulation in peripheral blood leukocytes. *J Thromb Haemost*

Submitted
**Kline JA**, Peterson CE, Steuerwald MT. Prospective evaluation of real-time use of the pulmonary embolism rule-out criteria in an academic emergency department *Acad Emerg Med*


Watts JA, Marchick MR, **Kline JA**, Pathophysiology of right ventricular injury from chronic versus acute occlusive pulmonary hypertension. *BMC Resp Med*

Invited Commentary

Published Scientific Letters

Correspondence
Kline JA, Right ventricle remodeling and elevated D-dimer concentration in patients 6 months after first episode of acute pulmonary embolism: reply. Eur Heart J. 2008
Kline JA. Reply to: Right ventricular remodeling and elevated D-dimer in patients six months after first episode of acute pulmonary embolism. IN PRESS Eur Heart J. 2008.

Other publications:
ACP Journal Club. Accuracy of the alveolar deadspace and D-dimer for diagnosis of pulmonary embolism. September 2001

Peer-review Responsibilities
JOURNALS
Cardiovascular Research, 1996-present
Academic Emergency Medicine 1997-present
Outstanding reviewer recognition 2001
Annals of Emergency Medicine, 1998-present
Top 50 Consultants recognition 2001
Top 50 Consultants recognition 2002
Top Peer Reviewer recognition 2005
Top 50 Consultants recognition 2007
Chest, reviewer 1998-present
Outstanding reviewer recognition 2000
JACC regular reviewer 2006-present
Thrombosis Research, Core reviewer 2004-present
Clinical Chemistry reviewer 2004-present
Clinical Physiology Ad-hoc reviewer 2004-present
Journal of Thrombosis and Haemostasis, Core Reviewer 2003-present
Thrombosis and Haemostasis, Core reviewer 2002-present
Critical Care Medicine, Ad-hoc reviewer 2001-present
American Journal of Physiology, Ad-hoc reviewer 2001-present
Kidney International, Ad-hoc reviewer 2001-present
Heart, Ad-hoc reviewer 2000-present
Am J Resp Dis Crit Care Med 2008
JAMA 2009
Annals Internal Medicine 2009

EDITORIAL BOARD APPOINTMENTS
Academic Emergency Medicine-Senior Associate Editor 2006-present
Academic Emergency Medicine-Associate Editor 2002-2006
Academic Emergency Medicine-Editorial Board 2001-2002
Emergency Medicine Australasia-Editorial Board 2008

ABSTRACT REVIEW FOR NATIONAL MEETINGS
Society for Academic Emergency Medicine 1997-present
American College of Emergency Medicine 1999-present

GRANT REVIEW COMMITTEES
Emergency Medicine Research Fellowship

**Society for Academic Emergency Medicine**
- Resident Research Award (Chair) 2000
- Research Sabbatical Award 1999

**Emergency Medicine Foundation (ACEP)**
- Chair, Scientific Review Committee 2006-present
- SRC Basic science committee Chair 2004-2006
- Established Investigator Award (Co Chair) 2001
- FERNE Award 2001
- Career Development Award 2000
- Scientific Review Committee 1999-present
- Research Fellowship Award 1999

**National Institutes of Health**
- SCCOR special emphasis panel 2006

**Teaching Responsibilities:**
- Director, Pediatric Emergency Medicine Fellowship Research 2007-present
- Co-director *Evidence-Based Medicine Series*
  - Carolinas Medical Center 2004-present
- Co-director *Shock Week*
  - Carolinas Medical Center 2004-present
- Faculty ACEP Emergency Medicine Basic Research Seminar 2001-2005
  (Ethical and IRB issues in research; Setting up a research program)
- Coordinator, clinical skills laboratory
  - Carolinas Medical Center 1998-2000
- Director, Emergency Medicine Research Fellowship
  - Carolinas Medical Center 1996-present

**Scholarly courses/Regional meetings directed:**
- SAEM Mid-Atlantic Regional Research Meeting
  - Charlotte, NC April, 2001

**Educational Websites:**
- Studymaker CME series on pretest probability. [www.studymaker.com](http://www.studymaker.com)

**COMMERCIAL ENTITIES**

**Companies cofounded**
- BreathQuant Medical Systems LLC 2006-present
- Pretest Consult LLC 2005-present
- Breathquant Medical Systems Inc 2001-2006

**FDA Investigational numbers (sponsor and PI)**
- IND 100274 Randomized trial of tenecteplase to treat severe submassive pulmonary embolism
- IND 103280 Inhaled nitric oxide to treat acute pulmonary embolism
IDE 167856  Collection of exhaled breath condensate from patients with suspected pneumonia

**US Patents (as primary inventor):**

**Pending**
System and Method For Evaluating Pretest Probabilities of Life-Threatening Diseases
Continuation-In-Part #1: November 25, 2005. Serial number pending
(Vital sign lookup, medical record storage)

Utilizing Lipopolysaccharide in Exhaled Breath Condensate to Diagnose Gram Negative Pneumonia
Non-Provisional filing date May 23, 2005. Serial number 135265

System and Method for Noninvasive Detection of Airway Restriction
Nonprovisional filing date February 20, 2005 Serial number 11/282,012

Use of Free Hemoglobin and its Surrogate Markers to Detect and Monitor Pulmonary Hypertension.
Non-provisional filing date March 3, 2005. Serial number 071745

Network-based System and Method for Secure Collection and Study of Clinical Research Data
Non-provisional filing date July 1, 2004.

Disposable hand-held device for collection of exhaled breath condensate
Non-provisional filing date December 19, 2003 Serial number 742721
Notice of Allowance, Japan, 4,299,837

**Issued**
Device and Method for Collection of Exhaled Alveolar Breath Condensate

Non-invasive Device and Method for the Diagnosis of Pulmonary Vascular Occlusions
Status: Issued June 3, 2003 patent number 6,575,918
(Exhaled CO2/O2 ratio to diagnose pulmonary embolism)

Non-invasive Device and Method for the Diagnosis of Pulmonary Vascular Occlusions
US patent number 6,881,193
(Infusion and detection of exhaled inert gas)

Non-Invasive Device and Method for Measuring the Cardiac Output of a Patient
US Patent number 7,344,497

Non-invasive Device and Method for the Diagnosis of Pulmonary Vascular Occlusions
US Patent number 7,104,964
(Mass spectrometer to detect nitrogen)

Non-invasive Device and Method for the Diagnosis of Pulmonary Vascular Occlusions
US Patent number 7,445,601
(Nitric oxide, carbon monoxide, ozone, coordinate plot of CO2-O2)

Non-invasive Device and Method for the Diagnosis of Pulmonary Vascular Occlusions
US Patent number 7,066,892
(Measuring efficiency of alveolar ventilation)
Non-invasive Device and Method for the Diagnosis of Pulmonary Vascular Occlusions
US Patent number 7,083,574
(Monitoring response to resuscitation)

System and Method For Evaluating Pretest Probabilities of Life-Threatening Diseases
Non-provisional filing date: October 8, 2002. Serial number 267134
Notice of Allowance, Australia, 4/26/06 No. 20024200693

Registered US Trademarks
Wordmark “Carboximeter” Filing date April 19, 2004. Serial number 78410642
Wordmark “Carboximetry” Filing date April 19, 2004. Serial number 78410656
Wordmark “Pretest Consult” Filing date December 19, 2003. Serial number 78343198

Registered US Copyrights (as primary author):
Computerized Attribute Matching to Predict an Outcome
Electronic Form (“e-form”) For Secure Collection of Clinical Data Via the Internet

Individuals formally mentored in research since 1996
Michael R. Marchick MD. Research Fellow 2008-present. Major focus is role of hemeoxygenase-1 and pulmonary vascular stress response to acute pulmonary embolism.


Daren Beam MD. Medical Student, 2008. Project: Data collection for the PERC project and secondary analysis of immobility data. Funded by a Medical Student Award from EMF, 2007

Brad Stevinson, (MS3, Georgetown School of Medicine). Howard Hughes Medical Student Fellow, 2005-2006. Project title: Monocyte Chemoattractant Protein and Pulmonary Embolism. Status: Completed and published.


Research Fellow, 2002-3 Project title: Use of goal-directed ultrasound in undifferentiated circulatory shock. Status: Manuscript in press, Critical Care Medicine (see awards section). Funded in 2004 by Emergency Medicine Foundation Career Development Award (see grants section). Current Position: Assistant Director of Research, Department of Emergency Medicine, Carolinas Medical Center.


Andy Perron, MD, resident in Emergency Medicine 1997-98. Project title: Blood can be very bad: A mnemonic to improve cranial CT interpretation by emergency physicians.
Emergency Medicine Research Fellowship

Status: published Annals Emergency Medicine, 1998. Current position: Program Director, Department of Emergency Medicine, Maine Medical Center, Portland, Maine.


Research Narrative

Since 1999, my work has focused on screening, risk stratifying, and treating pulmonary embolism (PE). I have focused on PE because of its importance to society, and also because of the unique physiology that occurs with PE. I have investigated the role of using the alveolar deadspace (estimated using capnometry and arterial PaCO₂) plus a whole-blood D-dimer to screen for PE. At Carolinas Medical Center (CMC), we use a combination of a decision rule that I derived and the deadspace/D-dimer in what we term the “PE rule out” procedure. I then built and patented device to help diagnose and exclude PE based upon instant analysis of exhaled partial pressures of CO₂ and O₂. I co-founded BreathQuant Medical LLC (see www.breathquant.com), and spearheaded the formation of a joint venture between DEKA Research and Development, Carolinas HealthCare System, and WFD Ventures. Together, we have acquired $8MM in private funding and $850,000 from the NIH to launch a four center, FDA-regulated pivotal study of this device. This will be the first ever FDA-approved breath-based diagnostic device. Separately, I have a patent pending on novel method to quantitate pretest probability that I call attribute matching (US patent pending). The primary goal of this technology is to provide quantitative rationale for clinicians to not order an expensive test--such as computerized tomography. As PI, I received over $1MM in NIH funding to advance this technology. To help further the use of quantitative probability assessment in the real world, I recently applied to the American Medical Association for a CPT code to reimburse clinicians for the work required to use a multivariable model to assess probability of disease at the bedside.

Additionally, I have studied mechanisms of right ventricular damage from PE and I am keenly interested in methods to risk stratify and treat PE. In the laboratory, we actively use a rat model of PE that I developed to study the role of neutrophils in producing right ventricular damage from severe PE. I received my first NIH R01 to study novel biomarkers to prognose submassive PE, and I have incorporated findings from that project into a six-center RCT of tenecteplase to treat submassive PE.

I have tried to maintain a presence in the world’s medical literature inside and outside of emergency medicine. Over one-half of my publications are in non-emergency medicine journals. 90% of my publications are as first or senior author, and in journals with an impact factor above 2.0. From a research standpoint, I am most proud of my role as a mentor in stimulating the professional development of others. I have trained 8 research fellows in emergency medicine; six of whom are in academic practice. In 2005-2006, I oversaw Brad Stevinson, a medical student who worked with me for a year under a Howard Hughes Research Fellowship, which resulted in two publications for Brad. I am a preceptor on two funded K23 awards for two of my former research fellows. I have served as a project mentor on five resident research awards, one fellowship award, and two career development awards.
GRANTS
ACTIVE
R18HS018519-01 AHRQ $1,049,113.00
Quantitative Pretest Probability to Reduce Cardiopulmonary Imaging in Low Risk Patients with Chest Pain
Role: PI
Score 165, 3rd%ile
Major goal is to randomize 500 low-risk chest pain patients to either receive or not receive the results of a computerized pretest probability device and measure medical resource use.

P1 NIH/NHLBI1R01HL085565-01A2 $295,200
Outpatient Treatment of Low-Risk Patients with Pulmonary Embolism
Role: Site PI
Pending
Major goal is to test the feasibility of a score system to classify ED patients with PE into a low-risk group, initiate fractionated heparin and warfarin-sodium treatment and discharge. (PI: Don Yealy, Pittsburgh, PA)

Prediction of Moderate to Severe Post-thrombophlebitic Syndrome After Acute Deep Venous Thrombosis of the Leg, 7/1/2009-6/30/2010
Sponsor: Emergency Medicine Foundation Role: Mentor and Preceptor
Amount: $5,000
Goal: Develop a clinical laboratory to study patients with acute DVT

Randomized Trial of Tenecteplase to Treat Submassive Pulmonary Embolism
Sponsor: Jeffrey A. Kline
Funding agency: Genentech
Role: PI
Goal: Test the treatment efficacy of tenecteplase for submassive pulmonary embolism
Amount: $545,800

NIH/NHLBI
Fast-track R42 HL086316-01 $849,005 25-40% Effort
Expired CO2/O2 to diagnose pulmonary embolism 8/1/06-12/31/10
Role: PI
Major goal is to test the diagnostic accuracy of a breath device for diagnosis of pulmonary embolism.

K23 GM076652-01 NIH/GMS
1/1/06-12/31/11 $625,050 5% Effort
Project Title: Randomized Clinical Trial for a Non-invasive Resuscitation Protocol for Sepsis
Role: Project Preceptor/Mentor (Alan Jones PI)
Major goal is to provide clinical research training to Alan Jones and to develop a simple protocol to treat patients with sepsis syndrome in the emergency department

PENDING
RC3 AI089137 NIH/NIAID
Breath-based diagnosis of gram negative pneumonia
Role: PI
Major goal is to build and test a method including a device that captures exhaled breath condensate followed by lipopolysaccharide measurement to diagnose pneumonia.
1R01GM092871-01 – Glucose-insulin-potassium for the treatment of vasopressor dependent septic shock (Jones AJ, PI) $3,324,078
Role: Co-I
Major goal is to test the effect of GIK on time to vasopressor independence in humans with septic shock.

Not funded
AHA Fellow-to-Faculty Award
Hemeoxygenase induction as an adaptive response of the right ventricle during acute pulmonary embolism
Role: Mentor
Major goal is to test if inducible hemeoxygenase confers cytoprotection to the right ventricular muscle during acute pulmonary hypertension caused by acute pulmonary embolism.

RC1HL099804-01 NIH/NHLBI
Randomized Trial of Tenecteplase or Placebo to Treat Severe Submassive Pulmonary Embolism
Role: PI
Phase III Six-center study of tenecteplase to treat pulmonary embolism

R01 NIH/NHLBI
Biphasic effects of leukocyte recruitment during chronic pulmonary embolism
Role: CoI
Major goal is to determine the effect of inhibiting neutrophil-mediated injury on right ventricular function after severe pulmonary embolism in rats

COMPLETED
K23 HL077404-02 7/1/04-6/30/09 NIH/NHLBI, $586,508.00. Pretest probability assessment and D-dimer testing for PE (Courtney DM, PI). Role: Mentor
Major goal was to develop and validate a clinical instrument to allow safe D-dimer testing in the emergency department

North Carolina Small Business Program—STTR Matching Award (PI: Kline) $54,305


EMF Riggs Family Grant (PI: Kline), 2006-2007, $49,398, Randomized Trial of Pretest Probability in Low Risk Patients with Chest Pain, Major goal was to test the effectiveness of a computerized pretest probability device on patient safety and resource use

EMF Resident Research Grant (Preceptor: Kline), 2006-2007, $5,000, Venous Ultrasound to Diagnose and Exclude Deep Vein Thrombosis in the Emergency Department, Major goal was to measure diagnostic accuracy of EP-performed 3-point compression ultrasound for DVT

Charlotte-Mecklenburg Health Services Foundation Award (PI: Watts), 2005-2007, $14,843,
Chronic pulmonary hypertension in rats

Charlotte-Mecklenburg Health Services Foundation Award (PI: Zagorski), 2005-2006, $37,550,
Gene expression patterns in hypertensive right ventricles during acute pulmonary embolism
Charlotte-Mecklenburg Health Services Foundation Award (PI: Zagorski), 2005-2007, $19,914. Inhibition of leukocyte chemotaxis into cardiac tissue during acute pulmonary hypertension

NIH/NHLBI R42 HL074415-02A1 (PI: Kline) 2004-2007, $1,120,992. Pretest Probability Assessment for Pulmonary Embolism: Phase II. The major goal of this project was to collect data from 6000 patients undergoing evaluation for PE in the emergency department.

NIH/NHLBI, R01 HL074384-01 (PI: Kline) 2003-2007, $1,084,007. Surrogate Markers for Severe Pulmonary Embolism. The major goal of this project was to test the utility of noninvasive methods of risk-stratifying patients with diagnosed pulmonary embolism.

Kenan Collaborative Funding Award (PI: Kline) 2004-2006, $150,000.00/$30,000.00. Breath Condensate Analysis to Diagnose Pulmonary Embolism; Goal was to develop a noninvasive device to diagnose pulmonary embolism.

Kline Biosite Incorporation Contract 2002-2006. Contract amount $68,000.00. Right Ventricular Strain in Pulmonary Embolism (the RVSPE study). Deliverables were plasma samples from patients with diagnosed pulmonary embolism. Role: PI

Biosite Inc Contract: Sample Collection for Pulmonary Embolism 2005-2006. Contract amount $176,284. Major goal was to collect plasma from 175 patients with suspected pulmonary embolism. Role: Co-PI

Howard Hughes Medical Institute Research Training Fellowship for Medical Students 2005-2006. Award amount: $28,500. Project title: Role of MCP-1 in Right Ventricular Dysfunction after Pulmonary Embolism. Role: Project Mentor (PI: Brad Stevinson). Major goal was to test the effect of MCP-1 receptor antagonism on right ventricular function after experimental pulmonary embolism. Role: PI

Career Development Award (Mentor)/Emergency Medicine Foundation 2004-2005. Award amount: $50,000.00. Project title: Diagnostic Significance of Nontraumatic Emergency Department Hypotension. Goal was to determine the sensitivity and specificity of hypotension for in-hospital death. Role: Mentor and preceptor.

Research Fellowship Award (Mentor)/Emergency Medicine Foundation 2004-2005. Award amount: $75,000.00. Project title: Pulmonary Vascular Hyperplasia in Pulmonary Embolism. Goal was to determine extent and cause of pulmonary vascular remodeling after autologous PE in rats. Role: Mentor and preceptor.


NIH/NHLBI STTR 1 41 HL074415-01. Project title: Pretest Probability for Pulmonary Embolism 2003-2004. Award amount $106,482.00. The major goal of this project was to develop and test a PDA-web-based mechanism for clinical data collection on patients with suspected pulmonary embolism. Role: PI.

EMF Established Investigator Award, 2000-2001. Project title: Rapid Exclusion of Pulmonary Embolism (The REPE study) Award amount: $50,000.00. Role: PI


Novametrix Corporation Unrestricted Academic Grant, 1997-98. Project title: Development of CO₂ Lung Scan for Pulmonary Embolism: Phase I. Award amount $7,500.00. Role: PI.

EMF/SAEM Innovation in Medical Education Grant. 1996-97. Blood Can be Very Bad: A Mnemonic to Improve the Accuracy of Cranial CT Interpretation by the Emergency Physician. Award amount $5,000.00. Role: Preceptor.
American Heart Association Grant-in-Aid, 1997: Heart function after hemorrhagic shock: role of fatty acids, glycolysis and respiration. Award amount $55,000.00. Role: PI

Emergency Medicine Foundation Career Development Award. Project title: Effect of Insulin Treatments During Cardiovascular Depression Induced by Verapamil in the Chronically Instrument Canine: Comparison to Epinephrine and Glucagon. Performed at Carolinas Medical Center, 1994-1995. Award amount $25,000. Role: PI


A. D. Williams Foundation Award for Doppler – Echocardiographic Research. Conducted in the summer of 1988 at the Medical College of Virginia. Collaborated with James Arrowood, MD, FACS. Award amount $1750.00. Role: PI

Grants Submitted but not Funded:
National Institutes of Health, K-O8 Mentored Clinical Scientist Award. Heart Lung and Blood Institute. Project Title: “Regulation of Myocardial Dehydrogenase in Shock.” Role: Principle Investigator. Award Amount $401,000.00. Triaged without score


American Heart Association Regional Fellowship Award. The PEARREST study. Amount: $50,000.00. Role: Mentor. Score: 2.39

EMF Directed Research Award: Cardiac Arrest Survival Award. “Early Detection of Fatal Pulmonary Embolism” Role: PI. Amount: $100,000.00. Score 2.36

ACEP Research Fellowship Training Award. “Use of goal-directed ultrasound in undifferentiated circulatory shock” Role: Mentor. Amount: $35,000.00 Score 2.65

STTR Phase I Award. Exhaled Breath Condensate to Diagnose Pulmonary Embolism. $100,000.00; Triaged.

INVITED PRESENTATIONS

Community Presentations
- St. Marks Methodist Church. Pulmonary Embolism in Women, August 9, 2004, Charlotte, NC.
- Hawthorne Lane United Methodist Church. The Physical Death of Jesus Christ. Easter, 2007

International Presentations
• 5th Mediterranean Emergency Medicine Congress, Valencia Spain, September 13-18, 201-. Track Chair, Pulmonary Emergencies.

National Presentations:
• ACEP Scientific Assembly Faculty. Course title: “Shock” September 1996, New Orleans, LA.
• SAEM Annual Meeting Didactic Session. “Septic Shock in the Emergency Department From Bench to Bedside” May 2001, Atlanta, GA. Role: invited speaker
• ACEP Scientific Assembly Faculty. Course title: “New Standards in Cardiopulmonary Resuscitation” September, 2001, Chicago, IL.
• ACEP Scientific Assembly Faculty. Course title: “Name that Cranial Nerve,” September, 2001, Chicago, IL
• SAEM Annual Meeting Didactic Session: Coping with grant rejection. May 2002. Role: Session director. Sponsor: Research Committee
• SAEM Annual Meeting State of the Art Didactic Session: New Methods, Markers and Devices to Diagnose and Risk-Stratify non-traumatic Circulatory Shock. Role: Moderator and speaker. May, 2005
• SAEM Annual Meeting didactic session co-presenter: Registry Data: On Trial. Role: Speaker. May, 2005
• EmCare’s National Medical Director’s Conference, Dallas, TX, November, 2005. “Bedside diagnosis in the emergency department” Role: Keynote Speaker
• AAEM Scientific Assembly, San Antonio, TX, February 2006. “Five cases, five controversies in diagnosis and treatment of pulmonary embolism”
• SAEM Annual Meeting, didactic session co-presenter. “Performing industry-funded clinical trials.” May, 2008, Washington DC.

Regional Presentations
• SAEM Southern Regional Meeting "Funding in Emergency Medicine," Spring, 1998
• Carolinas Medical Center, Spring Symposium, “New Diagnostic Tests for Pulmonary Embolism.” Charlotte NC. May, 1998
• Panelist “Decision Rules from the North and South.” April 2005, Southeastern Regional SAEM Meeting.
• Carolinas Medical Center CME course Venous Thromboembolism November, 2008 “Fibrinolysis for submassive pulmonary embolism: a debatable indication whose time has come”

Keynote Presentations
• New York SAEM Regional Meeting, March 24, 2007. “Five Reasons to Do a Research Fellowship”
• Indiana ACEP Educational Meeting, April 2008. “Controversies in Venous Thromboembolism.”

Grand Rounds/Visiting professorships:
• University of Delaware Department of Emergency Medicine, “Cranial CT Interpretation for Emergency Physicians: Use of a mnemonic to improve interpretation skills” January, 1997;
• Medical College of South Carolina Department of Emergency Medicine, “Cranial CT Interpretation for Emergency Physicians: Use of a mnemonic to improve interpretation skills” March, 1997.
• Cannon Research Grand Rounds Seminar “From Roadside to Bench: Emergency Medicine Research” Charlotte, NC. August, 1999,
• Department of Emergency Medicine Grand Rounds. “Screening for Pulmonary Embolism in the Emergency Department.” September, 2000, University of Virginia, Charlottesville, VA.
• Northwestern University School of Medicine, Division of Emergency Medicine Grand Rounds and Visiting Professor. “Screening for Pulmonary Embolism in the Emergency Department” Chicago, IL. May, 2001.
- Department of Emergency Medicine Grand Rounds and Journal Club, State University of New York Downstate Medical Center: "Recent Advances in the Diagnosis and Treatment of Pulmonary Thromboembolism." Brooklyn, NY, September 2002.
- Department of Emergency Medicine Grand Rounds at Christiana Care Healthcare Systems: "PE Diagnosis and Management," October 2002, Newark, DE.
- Department of Emergency Medicine Grand Rounds and Visiting Professor, Massachusetts General Hospital: "New Advances in the Diagnosis and Treatment of Pulmonary Thromboembolism" October 2002, Boston, MA.
- Department of Emergency Medicine Grand Rounds. “Pulmonary Embolism: Research You Can Use.” September 2004, University of Virginia, Charlottesville, VA
- Department of Emergency Medicine Grand Rounds, March 2005. Albert Einstein School of Medicine, Philadelphia, PA.
- Department of Emergency Medicine Grand Rounds, August, 2005. “Initial Approach to Pulmonary Embolism at the Bedside.” Maine Medical Center, Portland, ME
- Department of Emergency Medicine Grand Rounds, October, 2005. “Initial Approach to Pulmonary Embolism.” Brown University Department of Emergency Medicine, Providence, RI
- Department of Emergency Medicine Grand Rounds, October, 2006. “Diagnosis and Treatment of Pulmonary Embolism in 2006” and “Overtesting in Emergency Medicine: The Unpublished Epidemic” Methodist Hospital/University of Indiana School of Medicine, Indianapolis, IA.
• Department of Emergency Medicine Grand Rounds, October, 2007. “Exclusion of Fatal Disease at the Bedside” Vanderbilt School of Medicine, Nashville, TN.
• Department of Emergency Medicine Grand Rounds, University of California, San Diego, June 17, 2008
• Department of Emergency Medicine Grand Rounds, University of Iowa: #1 The pivotal role of research in a world-class emergency medicine training program. #2 Screening, diagnosis, risk-stratification, anticoagulation and fibrinolysis for pulmonary embolism: five key questions (and five answers that are at least partially correct), April, 2009.
• Department of Emergency Medicine Grand Rounds, Northwestern University. Fibrinolysis to treat submassive pulmonary embolism. March, 2009

Seminar and colloquia:
• “Myocardial energy transfer in circulatory shock” UNCC Department of Biology graduate school seminar, October, 2000.
• “Issues in technology transfer: from concept to licensing” BIOL 8200 UNCC Biomedicine and Biotechnology PhD core colloquium lecture, November, 2001.
• “Cause and effect of right ventricular damage from pulmonary embolism: perspective of a translational researcher.” Maine Medical Center Research Institute, December, 2005.
• “Pretest probability as a solution to healthcare expenditures wasted on unnecessary diagnostic testing” Blue Cross Blue Shield of Tennessee, Chattanooga, TN, January, 2006.
• “Automated methods to reduce unnecessary diagnostic testing in medicine” Machine Learning 6010, University of Tennessee, Chattanooga, January, 2006.
Biosketch
Dr. Kline received his medical doctorate from the Medical College of Virginia in 1990. He completed residency training in emergency medicine at the Carolinas Medical Center in 1993 and then a research fellowship in 1994. Dr. Kline’s research fellowship and early research career focused on cardiac contractility and energy metabolism in shock states. This interest led Dr. Kline to focus on cardiopulmonary stress induced by severe pulmonary embolism. He developed and published a rat model of pulmonary embolism and subsequently began clinical studies using breath-based methods to diagnose and assess the severity of pulmonary embolism in humans. His research interest has expanded to include the development of breath-based devices to diagnose PE and computerized devices to predict pretest probability. He has written 16 US patents for novel medical devices. To help translate these ideas into practice, he cofounded BreathQuant Medical Systems Inc, a privately held medical device company, currently supported by substantial venture capital funding. Over the past 7 years, he has published over 75 original manuscripts as first or senior author in the area of pulmonary embolism, and has trained 9 research fellows, all of whom hold faculty positions in emergency medicine. In 2004, he was elected to a three-year term on the Board of Directors at SAEM, followed by 2 years as Secretary-Treasurer, and in 2009, he was elected President Elect. He has received the National research awards given by ACEP and SAEM. He is or has been PI on three NIH/NHLBI-sponsored grants, including an R01, an R42 and a Fast-track R41/R42; he is the mentor on two NIH-funded K23 grants to two former research fellows, and has received funding from the Howard Hughes Medical Institute to serve as mentor for a Medical Student Research Fellowship. He resides in Charlotte NC, with his wife Judy, and two children, Hannah (15) and Paul (11).