younger ones are grafted onto them. This aspect of identity maintenance is of importance for vessel transplantation.¹⁻³

It is interesting to note that neo- and revascularization in postnatal life share many, if not all, of the above-described mechanisms and altering these is the basis of novel angiogenic or antiangiogenic therapies and, in the future, vessel-remodeling treatments. Blood vessels do not seem to have the luxury of asking themselves: to be or not to be? Their destiny is determined even before they are formed.

M. Castillo

H. Alvarez

University of North Carolina

Chapel Hill, North Carolina

References

1. Hirashima M, Suda T. Differentiation of arterial and venous endothelial cells and vascular morphogenesis. *Endothelium* 2006;13:137-45
2. Swift MR, Weinstein BM. Arterial venous specification during development. *Circ Res* 2009;104:576-88
3. Lamont RE, Childs S. MAPPING out arteries and veins. *Sci STKE* 2006;335:39
4. Aitsebaomo J, Portbury AL, Schisler JC, et al. Brothers and sisters: molecular insights into arterial-venous heterogeneity. *Circ Res* 2008;103:929-39
5. Larrive B, Freitas C, Suchting S, et al. Guidance of vascular development: lessons from the nervous system. *Circ Res* 2009;104:428-41
6. Adams RH, Alitalo K. Molecular regulation of angiogenesis and lymphangiogenesis. *Nature* 2007;8:464-78
7. Mancini ML, Terzic A, Conley BA, et al. Endoglin plays distinct roles in vascular smooth muscle cell recruitment and regulation of arteriovenous identity during angiogenesis. *Dev Dyn* 2009;238:2479-93

DOI 10.3174/ajnr.A2266

EDITORIAL

Searching the *Journal* for Evidence-Based Radiology

In the past several years, major concern has been raised from both quality and safety advocates and third-party payers regarding medical practice patterns with excessive use of imaging. As health care reform is upon us, it has become particularly important to substantiate medical imaging for specific clinical conditions. This is coupled with the increasing public awareness and concern regarding the risks from medical imaging, especially radiation exposure. As radiologists, we are now expected to provide even more information to our patients, referring physicians, and payers. This information may be partly based on our practice experience, expert opinion, and sometimes the available published literature. However, more recently, scientific evidence is being emphasized as a major component in guiding medical decisions. Thus, the practice of evidence-based radiology has emerged as the application of the best available scientific evidence to patient care.

Evidence-based radiology is a valuable method to use when a specific clinical problem arises that initiates a literature search for additional scientific information. Critical thinking skills are necessary to appropriately gather this relevant literature and interpret its scientific merit by using established methods and criteria. Medical decisions can then be based on the most valid scientific evidence available. This process describes a bottom-up approach for problem-based learning, first developed by McMaster Uni-

versity and the Center for Evidence-Based Medicine, Oxford. The evidence-based radiology Web site developed by Malone et al¹ is an international effort to help radiologists who have no specific training in research to use the principles of evidence-based medicine in answering clinical questions in their practice. An established method described for practicing evidence-based radiology has been developed by Sackett et al² with the following 5 steps: 1) "Ask" describes how to structure a clinical question into an answerable format. 2) "Search" describes how to perform a comprehensive literature search relevant to the question. 3) "Appraise" describes how to critically evaluate the literature by assessing its validity, reliability, and usefulness. 4) "Apply" describes how to use these results in the care of patients. 5) "Evaluate" describes a self-evaluation process for improving critical thinking skills.

These 5 steps are a useful guide for radiologists in implementing evidence-based radiology in their practice. To obtain a relevant literature search for a clinical problem, one must structure the question to contain certain components by using the Patient, Intervention, Comparison, and Outcome format. For example, a clinical problem in imaging patients with acute stroke is deciding between using CT perfusion or MR perfusion for evaluation of ischemic penumbra. The question should include the following terms: the specific Patient population as "patients with acute stroke" AND the Intervention as "CT perfusion" AND its Comparison as "MR perfusion" AND the desired Outcome as "ischemic penumbra." The question may be phrased as the following: In patients with acute stroke, is CT perfusion better at diagnosis of ischemic penumbra than MR perfusion? The search text for this example would be "acute stroke AND CT perfusion AND MR perfusion AND ischemic penumbra." This structured question lends itself to a reproducible search of the literature that yields fewer but more relevant research articles.

Commonly, search engines such as PubMed, Ovid, Knowledge Finder, and Google Scholar are used to explore the large electronic databases of MEDLINE, EMBASE, Cochrane, and the Web of Science. Other resources include using the related articles featured in PubMed for all references as well as the reference lists of all relevant publications. Additional information may be gathered by contacting the authors or experts in the field. A librarian is an excellent resource to assist in searching your question, especially for expanding your search strategy.

Once the relevant research articles have been obtained, review and appraisal of the literature are performed. The research articles are ranked according to hierarchic scientific evidence by analyzing the Methods and Results sections. Levels of evidence have been defined on the basis of the validity of the Results and the possible sources of bias in the Methods. The base of the pyramid (level 4) is considered the lowest level of evidence and comprises the primary literature, such as original published research studies. There is wide variability in the evidence provided in original research, ranging from insufficient evidence (as seen in research with major study design flaws, case reports, observation studies, and expert reviews) to strong evidence (as seen in research with broad generalizability, prospective blinded clinical trials, and meta-analyses). The secondary literature comprises the top portion of the pyramid with evidence-based reviews, synopses, and information systems.

Level 3 contains the evidence-based reviews, such as systematic ones, which follow strict methodologic criteria in reviewing the literature for a specific clinical topic and thus provide more

reliable information than the traditional expert reviews. Level 2 contains synopses that summarize the results of systematic reviews in combination with the best current primary literature. The apex of the pyramid (level 1) contains the most valid evidence and comprises information systems that integrate and summarize all relevant and important research regarding a specific clinical topic.

The validity of a research article is based on how close the study results are to the truth. This can be determined by assessing the study design in the Methods section regarding the patient-selection process, reference standard, internal and external biases, and limitations. A level of evidence or quality scores can assist in determining the better quality research studies. An example is the Quality Assessment of Diagnostic Accuracy Studies appraisal tool,³ which can be used to evaluate research studies concerning the diagnostic accuracy of a test. The second part of the appraisal process is to assess the strength of the research findings by analyzing the Results section. The sensitivity and specificity, confidence intervals, positive and negative predictive values, and likelihood ratios are all used to assess the ability of a diagnostic test to reliably differentiate between disease and healthy status. The confidence interval around the sensitivity and specificity gives an idea of how close to the truth these results may actually be.

The application of the best evidence into clinical practice requires a transition from thinking about the sensitivity and specificity of a diagnostic test to the likelihood or probability of the patient having the disease. The “pretest probability” is the clinician’s estimate of the patient’s probability of having the disease, given all the available data. The “posttest probability” is simply defined as the pretest probability updated by the test results. If the pretest probability is above the clinician’s inclusion threshold for disease diagnosis or below the exclusion threshold, then no further diagnostic testing is necessary because there is a reasonable degree of certainty that the patient does or does not have the disease. However, between these thresholds is the uncertain area that warrants further diagnostic testing to move the patient’s probability of disease either above the inclusion or below the exclusion thresholds. The greater the strength a diagnostic test has with high sensitivity and specificity, the less influence the clinician’s pretest probability has in determining the patient’s disease status.

There are several limitations and barriers to implementing evidence-based radiology in practice. Getting started may be overwhelming because the critical thinking skill set required is relatively new to radiologists, and many do not have prior experience or training. Training courses, Web-based tutorials, and textbooks are available to learn more about evidence-based medicine. Another option to getting started is to work with a librarian. The expertise of a librarian is a valuable resource in performing a comprehensive search of the literature. Getting a librarian to also search your question can assist in identifying your knowledge gaps and the limitations in your search strategy, improving your skills.

Once you have overcome this obstacle of getting started, time limitation remains the main barrier to performing evidence-based radiology in practice. A valuable short-cut is to seek evidence from as high in the evidence pyramid as possible, such as the evidence-based reviews, systematic reviews, and meta-analyses. These structured reviews provide reliable

information by using strict methodology designed to limit bias. The relevant research is critically appraised, and the best evidence is summarized for you in these structured reviews. However, at times, the best evidence may not be readily available because there is a tendency not to publish “negative” studies in the literature. Last, case reports are considered as the lowest evidence in the pyramid; however, these reports may provide valuable information in specific clinical scenarios.

In summary, “evidence-based practice” is defined as “the integration of best research evidence with clinical expertise and patient values.” This requires the art of balancing the scientific evidence, clinical expertise, and judgment. When there is strong scientific evidence (at the apex of the pyramid) with information systems that summarize and integrate all relevant research about a clinical topic, then practice guidelines can be developed, and with time, these guidelines are implemented as standard practice. However, when only weak evidence is available, then clinical expertise and judgment become a major component guiding our medical decisions. Judgment is particularly important when the evidence is inconclusive because we rely on our judgment to detect differences between observations in research and to understand their significance in clinical practice.

Many times conclusive evidence is not available at the time a medical decision needs to be made because acquiring strong evidence is time-consuming and costly and may lack research interest. However, at the point-of-care level, a decision needs to be made regardless of the lack of knowledge and evidence available. Therefore, as difficult as it may be, sound clinical judgment may be most valuable in guiding patient care when only weak or inconclusive evidence is available.

References

1. Malone DE, Skehan SJ, MacEneaney PM, et al. Evidencebasedradiology.net. www.evidencebasedradiology.net. Accessed September 1, 2010.
2. Sackett DL, Richardson WS, Rosenberg W, et al. *Evidence Based Medicine; How to Practice and Teach EBM*. 2nd ed. Edinburgh, United Kingdom: Churchill Livingstone; 2000
3. Whiting P, Rutjes AW, Reitsma JB, et al. The development of QUADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. *BMC Med Res Methodol* 2003;3:25

P.C. Sanelli

Department of Radiology
New York-Presbyterian Hospital
Weill Cornell Medical College
New York, New York

DOI 10.3174/ajnr.A2390

EDITORIAL

Response Assessment in Neuro-Oncology Criteria: Implementation Challenges in Multicenter Neuro-Oncology Trials

The Response Assessment in Neuro-Oncology Criteria (RANO) Working Group recently published updated guidelines for assessing response to therapy in high-grade gliomas.¹ The goal of the group continues to be the development