RE-INVENTING RADIOLOGY IN A DIGITAL AND MOLECULAR AGE

Summary of Proceedings of the Sixth Bi-Annual Symposium of IS³R

August 25-27, 2005

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The International Society for Strategic Studies in Radiology is a non-political, not-for-profit organization whose purpose is to define and investigate strategic, scientific and economic issues of global importance to the field of radiology. The Society aims to foresee national and global developments in radiology and allied fields, and to strategically communicate important issues to radiologists, physicians in other medical fields, industry and governments. By forming a strategic partnership with industry in order to define important and relevant fields of cooperation and common engagement for the best possible cooperation and successful future of both partners, IS3R hopes to envision strategies for actively influencing research, clinical practice and teaching now and in the future, and to prepare radiologists, their partners, and their clients for future developments. The Society aims to influence the flow of capital and investment into the most scientific and strategic fields, and to influence health care politics for the benefit of radiology, its patients and customers.

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INTRODUCTION

Escalating costs and inadequate quality and safety are over-riding concerns of healthcare at this time. This is especially true in the United States, where more money is spent on healthcare than elsewhere and the health industry claims the largest section of the economy, greater than real estate. The increasing cost of healthcare worldwide can be attributed in part to the aging of populations but it is also due to the successful treatment of acute illnesses and the resultant shift towards the costs of caring for the chronically ill, which now accounts for 75% of the costs. But with healthcare costs at 14% of the GDP in the United States at present and projected increases to 18% by the end of the decade, there is considerable pressure from employers, insurance companies, and government to limit health care spending to a sustainable amount and to make the system more accountable. For example, the per person cost of healthcare in the United States is greater than the cost of steel in a car.[1] Yet, while steel quality is related to cost, the relationship between cost and quality in healthcare is hard to determine.

Overall, diagnostic radiology utilization rates increases have been modest in the United States, with a 3.1% compound annual increase for Medicare enrollees in the period 1992-2001 (1). However, utilization of high-cost radiology services increased dramatically in the past decade (Figure 1), as has been demonstrated for Medicare enrollees (1-6), privately insured groups (1, 3, 5), and within individual institutions (7, 8). Data for Medicare enrollees, which is more complete than that for other populations, show a trend of double-digit annual rate increases in utilization of CT, MR, and nuclear imaging in the years 1992-2001 (1). Data from the Medical Expenditure Panel Survey (MEPS), a nationally representative survey conducted by the Federal Government, indicated that the rate of MR imaging increased at an annual compound rate of 14.5% overall in the years 1996-1999, while the increase in those over 65 yrs was 19% (1). Similar patterns are seen in Europe and Asia. In one Munich hospital, CT examinations have doubled in the past 5 years, while MRA has increased from 600 to more than 3500 examinations per year and cardiac MRI from 25 to 190 per year.[2]

In 1990, the US costs of radiology accounted for about 3.5% of national spending on healthcare (9). Therefore, even allowing for a relatively high growth rate, radiology accounts for only a small proportion of the total costs of health care. Nevertheless, it is incumbent on radiology to minimize overuse and misuse of imaging procedures, while ensuring that patients who will benefit from radiological procedures do so.

The second major concern revolves around quality and safety. The rate of adverse events in medical care in the United States is 3-4% (10, 11), which, according to projections by the Institute of Medicine may result in as many as 44,000 - 98,000 deaths per year due to provider error and $28 billion in unnecessary expense (12). Again, converging forces from outside the healthcare provider network, including both the insurers and the public, are demanding change, e.g. http://www.leapfroggroup.org/home. In radiology practice, quality includes obtaining the best possible images through appropriate selection of modality and protocol, quality assurance programs that ensure optimal perform-

[1] Thompson, TG. IS3R Symposium, August, 2005
[2] Reiser, M. IS3R Symposium, August, 2005

ance of scanners, efficient work flow, timely completion of examinations and procedures, accurate diagnoses and prompt communication of reports to the referring physician. Safety issues include avoidance of injury due to the effects of magnetic fields on metallic implants, contrast agent reactions, or radiation exposure, and ensuring that there is adequate monitoring of patients for adverse events related to their medical conditions while in the care of radiology departments. Efforts to improve quality and safety require identification and mitigation of points of failure in work-flow processes and the practice of evidence-based medicine as far as possible. Information technology will be a major player in this process.

From the beginning, radiology has been a distinct medical specialty with unique technical challenges. The origins of specialization can be traced back to the technical nature of x-ray image capture and, perhaps more significantly, the difficulty of exposing, transporting, and developing images on fragile glass plates for subsequent interpretation. Despite pressure in the early 1900's to relegate radiology to a technical service, radiographic image interpretation and reporting required medically trained specialists. Therefore, radiologists have been clinical specialists who have been obliged to also become experts in image capture technology, broad based advances in engineering and, more recently, applications of information technology for health care, which continue to drive and be driven by radiology.

Computerization became an integral part of radiology with the advent of computerized tomography in the 1970's although the images were still printed on film for interpretation. By the end of the second millennium, computerized workstations were commonplace, picture archiving and communications systems (PACS) and radiology information systems (RIS) widespread, the internet was almost essential for transfer of images and other information, and computer aided diagnosis (CADx) was being developed as a useful tool. Molecular imaging, in which an agent that combines a moiety detectable by imaging with a moiety that binds to a molecular target in vivo, now brings radiology into the era of molecular medicine. All these factors suggest that radiology is well situated to be a driver in the transformation of medicine into the age of information technology and molecular medicine.

ADVANCES IN TECHNOLOGY DRIVE INCREASED UTILIZATION

As technology has improved, image acquisition has become faster and pixels have become smaller. This is especially true for CT (Table 1), as the number of detectors in the gantry has increased from one to four, sixteen, and now sixty-four while rotation speed has increased from 1 to .33 seconds/rotation. Image post-processing to yield 3D images or maximum intensity projections makes visualization clearer and provides more information than axial projections alone. Such advances provide new applications for radiology in, for example, cardiac imaging by making it possible to see not only the lumen through which blood flows but also atherosclerotic plaque that lines the blood vessel walls. Cine images can show real time motion of, for example, heart valve functionality. Computer reconstructed images can simulate colonoscopy. Non-invasive imaging techniques, such as CT pulmonary angiography, are much easier and safer than catheter-based techniques. PACS technology and electronic communication shortens the wait for radiology reports from days to hours or even less (13, 14). As a result, the threshold for ordering a study is lowered.

With so many technological advances, it is not surprising that radiology utilization of high-cost studies such as CT and MRI is expanding rapidly worldwide. Overall, CT use increased in the United States from 9.2% to 15.3% of radiological examinations while plain film radiography dropped from 70% to 57.1% (Figure 1), (15). This has resulted in larger and more complex workloads but not proportionally higher costs to the consumer. In fact, radiology cost/service decreased 19% in inflation corrected dollars from 1992 to 1999 (16). The workload and complexity of radiology services has also increased in Europe. However, there are considerable differences in the utilization rates of high cost imaging not only among European countries but also between states in the United States – differences that do not necessarily reflect the quality of healthcare. In 2002, the rate of CT examinations varied from below 20 to about 120 per thousand population in European countries (17). In comparison, the CT utilization rate in the United States was reported to be 113 per thousand enrollees in one Health Maintenance Organization (HMO) in 1998 and 391 per thousand of those enrolled in Medicare in 1999 (1).

The number of radiologists in the Unites States has not increased at the same rate as the number of examinations. While the workforce has increased at a rate of 1 - 1.5% over the past decade, the average workload increased over the same time period from 11,100 to 13,900 procedures per year or 6,000 to 9,100 relative value units (RVU)/year (Table 2). This translates to a workload increase of 25.1% in terms of procedures per FTE and 52.2% RVUs/FTE from 1992 to 2002 (15). Despite this increase in workload, the shortage of radiologists does not appear to have worsened as judged by the number of job advertisements,[3] although shortages of manpower are found in certain specialties, such as mammography, vascular/interventional radiology, and pediatric radiology.[4] In Asia, the radiology workforce has increased significantly over the past few years but the number of radiologists is grossly inadequate in many countries (Figure 2), especially in rural districts because most radiologists work in the big cities.[5] Among European countries, there are considerable disparities in the radiology workforce (Figure 2) and teleradiology is in use to compensate for lack of local radiologists.[6]

There is also worldwide concern about the number of radiologists in training, which is grossly inadequate in several of the poorer Asian countries.[7] In Europe, several countries are not training enough radiologists to replace retirements. However, some countries that have a particularly low number of radiologists, such as Eire and the United Kingdom, are now training a relatively high number.[8] In the United States, the numbers of radiologists in training has increased back to the levels of the early 1990's but may not be sufficient to meet future demand.[9]

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[3] Sunshine, JH. IS³R Symposium, August, 2005
[4] Maynard, C. IS³R Symposium, August, 2005
[5] Tan, L. IS³R Symposium, August, 2005
[6] McCall, IW. IS³R Symposium, August, 2005
[7] Tan, L. IS³R Symposium, August, 2005
[8] Reiser, M. IS³R Symposium, August, 2005
[9] Reiser, M. IS³R Symposium, August, 2005

TABLE 1

Advances in CT Technology, 1980-2004

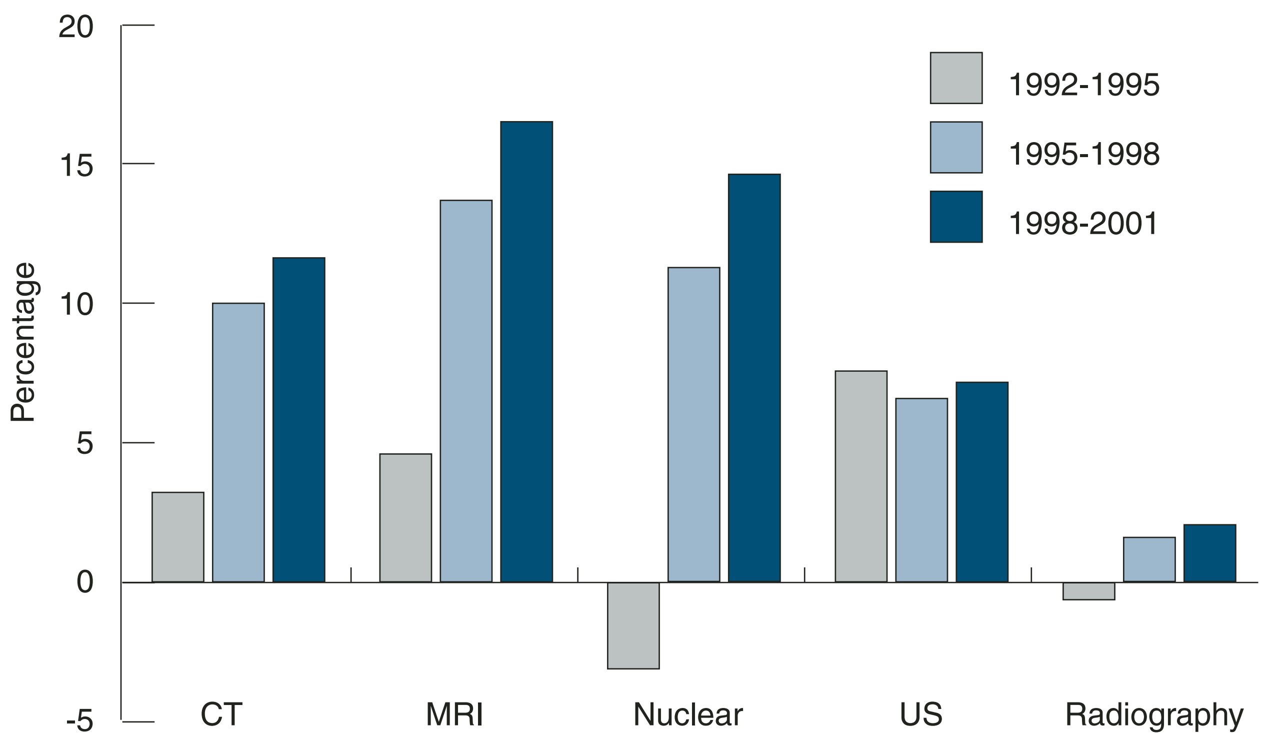
The CT Scan Journey Thru Time

year	Scan speed	Slice thickness	Interscan speed	Total # of slices
1980	10 sec	10 mm	10 mm	25-30
1985	5 sec	8-10 mm	8-10 mm	30-45
1990	1 sec	3-5 mm	3-5 mm	100
1995	.75 sec	3 mm	2-3 mm	100
1999	.5 sec	1-3 mm	1-3 mm	220
2003	.4 sec	.5-.75 mm	.5-.75 mm	400-1200
2004	.33 sec	.5-.6 mm	.5-.75 mm	600-4000

From Elliot Fishman; IS^{3}R Symposium, August, 2005

FIGURE 1

Trends in Radiology Utilization, 1992-2001



Data from Bhargavan and Sunshine, 2005 (1)

TABLE 2

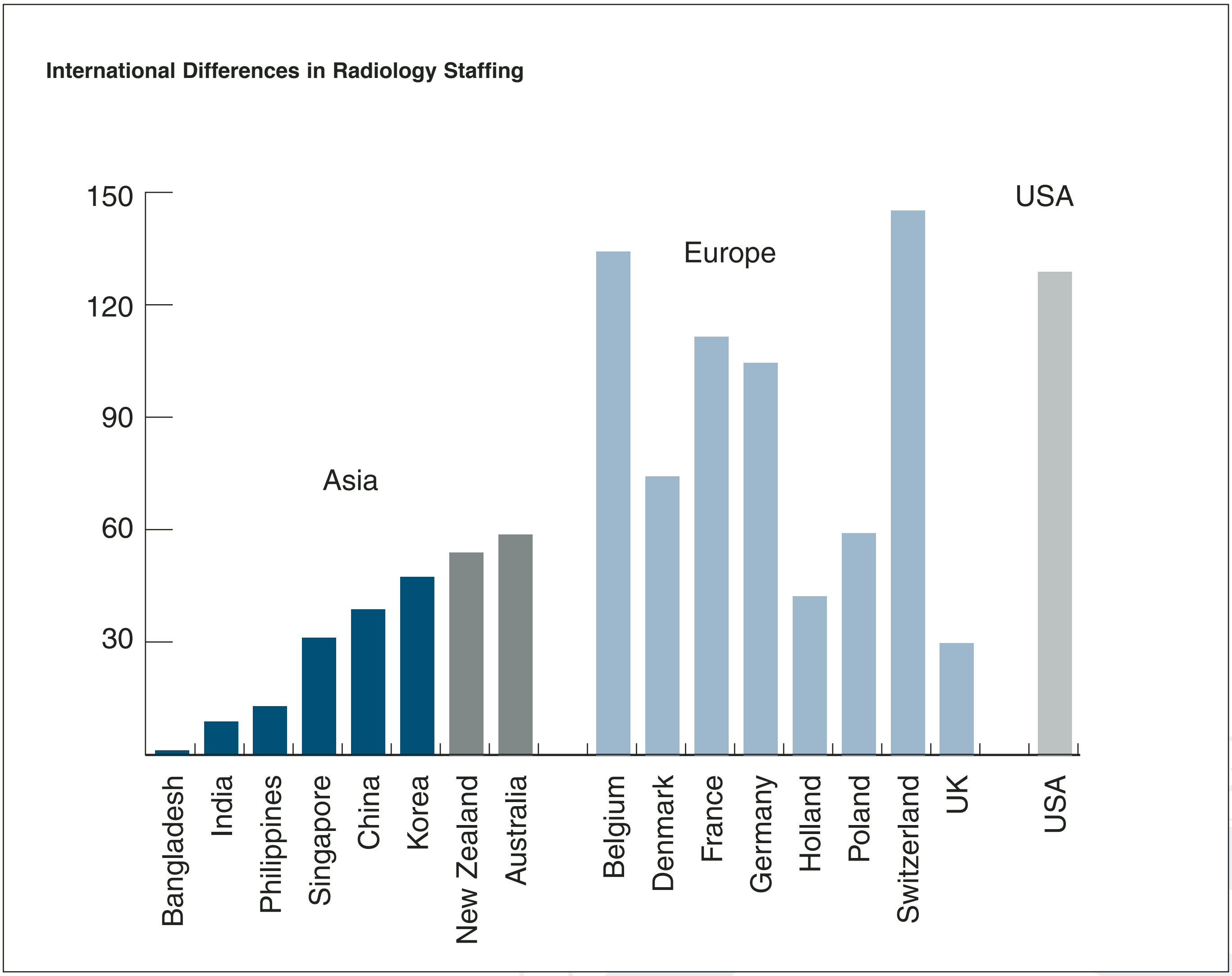
Summary of Growth Rates in Radiologist Workload in the USA 1992-2003

Parameter		Percentage Growth 2002-2003	1998-1999	1995-1996	1991-1992
Mean number of procedures per FTE*		13.9	12.8	11.8	11.1
Compound average annual growth since previous survey		1.6	3.0	1.9	
Compound average annual growth, 1992-2003	2.1%				
Total growth, 1992-2003	25.1%				
Median number of procedures per FTE*		13.4	12.7	11.4	11.0
Compound average annual growth since previous survey		1.0	3.7	1.2	
Compound average annual growth, 1992-2003	1.8%				
Total growth, 1992-2003	21.5%				
Physician work RVUs per procedure		0.65	0.62	0.57	0.54
Compound average annual growth since previous survey		1.2	2.7	1.9	
Compound average annual growth, 1992-2003	2.0%				
Total growth, 1992-2003	21.6%				
Estimated mean RVUs per FTE*		9.1	7.9	6.7	6.0
Compound average annual growth since previous survey		2.8	5.8	3.8	
Compound average annual growth, 1992-2003	3.9%				
Total growth, 1992-2003	52.2%				
Estimated median RVUs per FTE*		8.7	7.8	6.5	5.9
Compound average annual growth since previous survey		2.3	6.5	3.1	
Compound average annual growth, 1992-2003	3.6%				
Total growth, 1992-2003	47.9%				

* In thousands. Abbreviations: FTE, full time equivalent employee; RVU, relative value unit.

From Bhargavan and Sunshine, 2005 (15)

FIGURE 2



Data from McCall (17) and Tan, IS^{3}R Symposium, 2005

IMPACT OF DIGITAL IMAGING AND INFORMATION MANAGEMENT ON PRODUCTIVITY

That radiologists have been able to manage the increased workload can be attributed to improvements in workflow and productivity, due largely to digital technology. Digital imaging, computer workstations, speech recognition technology, picture archiving and communications systems (PACS), and the ease of communication via the Internet have all facilitated workflow. For example, PACS installations improve efficiency in a number of ways. Films no longer have to be carried to a reading room and hung. Previous patient images can be easily found and seen at the same computer workstation as the current images (13, 14). PACS also improves patient care though faster reading of images with fewer remaining unread and through the creation of prioritized work lists, which result in rapid interpretation of urgent cases. Faster diagnoses lead to prompt treatment and patient satisfaction. In addition, PACS has been shown to improve diagnostic accuracy (18). However, much must be done before the benefits of these systems can be fully realized. Only one-third of radiology practices in the USA have installed a PACS system, although another third have plans to purchase.[10]

Teleradiology increases productivity indirectly by reducing or eliminating the need for on-site radiologists in small hospitals and private practices during nights and weekends. The largest use of teleradiology is from base to home in both Europe[11] and the United States (19). A 1999 survey in the United States showed that 71% of multi-radiologist practices had teleradiology systems in place, using them to interpret 5% of their studies, while 32% percent of solo radiologist practices had systems in place, using them to interpret 14% of their studies (19). In both situations, teleradiology was in use primarily for on-call interpretation, although one fifth of the studies were for consultation or primary reading at a larger regional hospital with 24-hour radiology coverage, across borders, or across time zones. In some countries, teleradiology is used to compensate for a manpower shortage. For example, teleradiology is used to read some images generated in the United Kingdom by radiologists in Spain.[12] In much of Asia, most radiologists work in the cities and teleradiology allows them to provide services for patients in rural areas.[13]

Although turn around time for teleradiology can be rapid and was reported in one study to average 12.2 minutes with 99% of reports received within 1 hr (20) there are concerns about quality, both within countries and especially across international borders. An American College of Radiology (ACR) Task Force on Teleradiology has recommended that physicians reading studies on US patients while outside the Unites States should be licensed in the state(s) where the studies originated, be credentialed and afforded privileges by the healthcare institutions contracting them, and carry liability insurance (21). Nevertheless, oversight of radiology practices thousands of miles away is difficult and there are fears that they will not follow rigorous quality assurance procedures or observe privacy rules. On the other hand, when radiologists are reading images in daytime hours, they are more likely to be fully awake and alert.

Computer-aided diagnosis (CADx), which uses software to distinguish between normal and abnormal patterns and for image enhancement, has been developed to draw the attention of the radiologist to possible lesions for evaluation. Radiologists regard computer-aided diagnosis (CADx) as a time saver that is comparable to a second opinion rather than a replacement for radiologists. Accumulating evidence indicates that a radiologist with CADx is better than a radiologist or CADx alone. For example, detection of breast cancer from mammograms with CADx assistance has been reported to be 16-20% higher than with a radiologist alone, with more tumors detected at an earlier stage but no change in the pre-test prediction rate for biopsy (22, 23). The acceptance of CADx for mammography can be illustrat-

[10] Hricak, H. IS³R Symposium, August, 2005
[11] McCall, IW. IS³R Symposium, August, 2005
[12] Reiser, M. IS³R Symposium, August, 2005
[13] Tan, LKA, IS³R Symposium, August, 2005

ed by the fact that following reimbursement approval in 2001, the number of ImageChecker CADx installations increased from 200 to 1600 in 2005.[14]

CADx applications for diffuse lung disease classification have been developed and shown to be correct 88-100% of the time compared to a “gold standard” (24). Applications in the detection of pulmonary nodules in chest X-rays and chest CT are also promising. Currently, there is considerable work on the development of new selective enhancement filters to better distinguish blood vessels from nodules (25), for aneurysm detection (26), and for other abnormalities. A major goal for CADx is to reduce false positives without reducing sensitivity. A Massive Training Artificial Neural Network (MTANN) has been developed for this purpose (27), which is designed to detect differences between benign and malignant nodules (28, 29). In the future, CADx applications are likely for all imaging modalities, anywhere in the body. However, before CADx systems can be implemented, there is a need to provide clear evidence of clinical advantages and/or increased performance levels.

Speech recognition technology, first introduced in the 1990s, is steadily replacing audio recording and transcription for reporting. Audio reporting and transcription is slow and inefficient because, after transcription, radiologists have to review and correct reports before they are approved and sent to the referring physician. With speech recognition, dictated words are instantly seen on a computer screen and immediately edited by the radiologists. The efficiency of this process is a great improvement, which not only saves money but also speeds the generation of radiology reports from days to hours (30, 31).

Speech recognition technology requires additional radiologist time, especially during the learning process. However, newer software can “understand” contextual speech, learn words, and predict phrases based on previous speech, making it much easier to use than early systems. There is still a need to improve recognition rates (31). Currently, accuracy is estimated to be about 95-96% but is predicted to become better as technology improves. In comparison, a study of the accuracy of dictation and transcription showed that one third of reports had errors requiring editing and 6% had substantive errors (32).

Speech recognition technology is now adopted in about 40% of academic radiology and 16% of all radiology practices in the United States.[15] Implementation over a much wider range of radiology practices would clearly be beneficial to cost-effectiveness of healthcare. However, digital speech recognition has met with resistance, at least in part because the radiologist does not directly benefit from the change to a new system even though cost and time savings are beneficial to the practice or to a hoggspital entity. Therefore, before speech recognition systems are installed, considerable time and effort must be spent on overcoming radiologists' concerns as well as on providing the necessary infrastructure and training to use the new technology (33).

PACS provides management of stored images and facilitates post-processing of all types of images, as well as coregistration of images from different modalities. 3D and maximal intensity projections are much easier for the nonradiologist to understand and measurements, such as tumor volume, can be automated. PACS and RIS aid communication both within and outside the hospital or radiology practice by facilitating transfer of images and reports to all physicians involved in the patient's care. This decreases the need for personal consultation, which in one study was reduced by 82% for general radiography and 44% for cross-sectional imaging when a PACS system was installed, despite an increase in the volume of studies (34). However, ensuring clear, accurate, and timely communication between radiologists and referring physicians is still a challenge that must be addressed.

PACS and RIS provide an opportunity to develop computerized radiology order entry systems. Such systems can be more convenient than ordering by phone and can readily be coordinated with aids such as appointment reminders and instructions for patients. In addition, computerized order entry can minimize duplication of orders as well as aid referring physicians by giving them feedback on the appropriateness of a study for a given situation. Those physicians who persist in ordering apparently inappropriate imaging examinations can be identified and asked to justify their use of high-cost imaging.[16]

Finally, PACS and other digital applications can transform education for both medical students and residents. Computer images are far more versatile than printed im-

[14] Doi, K. IS3R Symposium, August, 2005
[15] Seigel, EL. IS3R Symposium, August, 2005
[16] Rosenthal, DI. IS3R Symposium, August, 2005

ages; they can be magnified, scrolled, and, if 3D, rotated to be viewed from different directions. Learning can be facilitated by online applications although this is only practical with high-speed connections. Case presentations are facilitated by the ease of finding images in PACS. Medical students learn about PACS as a fundamental part of their studies, knowledge that is becoming essential even for those who will not become radiologists. However, only 17% of medical schools in the United States require a clinical rotation in radiology.[17] This needs to change.

RADIOLOGY REPORTING AND COMMUNICATION

Despite the many changes in the practice of radiology, report format has changed little and a transcript of a nineteenth century report could be mistaken for one of today: a lengthy descriptive narrative covering indications for the study, observations, analysis/diagnosis, and recommendations for further imaging (if any). Other relevant information includes comparisons with previous findings, anatomic localization, and quality assurance indicators. Narrative reports may be combined with graphical elements, such as arrows on the images themselves. Although reports tend to be lengthy, the number of important concepts that are included is remarkably small, usually no more than 3-4 in a single report.[18] In the future, the number of concepts and findings may expand with the inclusion of functional (e.g. BOLD fMRI) and quantitative information, such as apparent diffusion constant and perfusion data. When molecular medicine becomes more widely adopted, reports may also be correlated with genomic, pharmacokinetic, and proteomic information.

The current narrative radiology report format is far from ideal. Reports tend to be defensive and straightforward diagnoses are rare. The language used is more suited to communicating with other radiologists than with referring physicians (35). The inefficiency of verbal reporting was a concern for some radiologists early on, and standardized forms first appeared by 1913. However, the verbal report remains the norm and BIRADS, which uses a numerical scale to categorize levels of suspicion, is one of the few examples of a structured report that is in common use today.

To maximize the usefulness of reports in the digital age, standard structural elements that use a common lexicon are needed. If the language were more standardized and the format organized, automated extraction of text would be simpler and speech recognition more accurate, which would decrease time spent in correcting reports (31). Development of a common lexicon would allow semantically organized electronic storage and indexing of report elements, which may be explicitly linked to the image itself. Reference terminology databases have already been developed (UMLS, SNOMED, RADLEX), although they still need improvement.[19] The addition of helpful information in texts or online is another useful element that is easily included in an electronic report.

Multimedia, multidimensional, and multidirectional communication is an essential part of clinical radiology and is crucial for the added value of radiology as a specialty. Failure in communication leads to patient alienation (36) and reduced quality of care. 70-80% of malpractice lawsuits involving radiologists cite communication problems (37). PACS systems minimize the numbers of unread images, and reports may be transmitted and available online, but there is still a need to ensure that reports reach ordering physicians, especially in emergent or other non-routine clinical situations (38). Direct communication with a referring physician in person or by telephone is recommended by the ACR (38) but can be difficult and time-consuming. Difficulties are compounded when medical care is not rendered by a single physician and the referring physician is not clearly identified, or if the referring physician is a surgeon who may take no responsibility for medical problems unrelated to the planned surgery.

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[17] Novelline, RA, IS3R Symposium, August, 2005
[18] Seigel, EL. IS3R Symposium, August, 2005
[19] Dreyer, KJ. IS3R Symposium, August, 2005

Therefore, it would be helpful to have a fail-safe system of communication that automatically acknowledges report receipt at the time that the referring physician opens the report file.

Direct contact with patients may reduce uncertainty and anxiety and, in the United States, is mandated for mammography, self-referred patients, and when imaging has been ordered by a third party, e.g. for the purposes of applications for life insurance or future employment (38). In Europe, national, local and hospital policies vary but EAR believes that radiologists should communicate findings to patients if they seek information. However, the issue of direct patient communication is under debate because of concern that radiologists are trained to render interpretations of radiologic studies but not to give medical advice or intervene in clinical management (37). However, others feel that since there is less communication between radiologists and referring physicians than in the past, it would be beneficial to have more contact with patients.

REDESIGNING PATIENT CARE THROUGH DATA-DRIVEN MANAGEMENT

PACS, RIS, and hospital information systems (HIS) contain a wealth of information that can be extracted and utilized to drive improvements in health care. However, communication between the different information systems used in patient care is poorly developed. Consequently, electronic health records are not available to be transferred from one institution to another but, if available, could improve treatment, especially in an emergency. HIS and RIS use variations of a standard protocol, Health Level-7 (HL7), an event driven text-based system, to store patient data and to communicate with billing systems. Imaging systems use a more readily queried standard system, Digital Communications in Medicine (DICOM), to store and retrieve both text and images. Although some custom software is available to translate information from HL7 to DICOM, customization of HL7 systems has made it a challenge to develop widely applicable software.[20]

Special software, such as LEXIMER, has been developed that can analyze and classify unstructured radiology reports based on the presence of key words for clinically important findings, descriptors of severity, and recommendations (39). Data mining of this sort can generate huge amounts of information for the purposes of quality and safety management in radiology practices as well as the generation of teaching files, retrieval of previous images of unusual medical conditions to aid in diagnosis, and for the development of evidence-based medicine.

The potential value of standardized health care information exchange and interoperability between providers and others in the health care industry is enormous. Savings would accrue through avoidance of test duplication, drug interactions and other adverse drug effects, and simplification of record chart handling. The net value of savings from avoidance of duplication of radiology examinations alone is estimated to be $8 billion per year in the United States (40). Achieving these savings will require investments in interfaces to translate heterogeneous electronic vocabularies and to develop seamless integration with both local and remote medical records. This level of interoperability cannot be achieved without strong national leadership, investment, and policy incentives to develop national, or better, international standards. Without such leadership, non-standardized solutions are more likely to be developed, which will lock in local solutions, save less money, and ultimately cost more to convert to a fully integrated system.

Information technology can not only speed workflow and reduce paperwork, it can also be used as a source of data to examine workflow processes and outcomes. Analysis of data extracted from PACS and RIS systems can show where errors are generated and delays are caused as well as minimize overuse, under use, and misuse of radiological procedures. At Massachusetts General Hospital, data mining is already in use to optimize radiology workflow by allowing radiologists to select cases for severity or prior recommendations, to summarize previous findings, and display missed recommendations.

[20] Dreyer, KJ. IS3R Symposium, August, 2005

QUALITY AND SAFETY ISSUES

A quality radiology practice will consistently perform the right procedure at the right time for the right patient, deliver radiology reports that are timely and accurate, and provide the patient with optimal personal care. However, this ideal is not reality and, as mentioned above, the number of adverse events occurring due to medical mistakes is unacceptably high (12). Even 99.99% reliability in a large practice will result in a significant number of adverse events. Of course, no one in medical care wants to make mistakes and everyone involved experiences anguish if an adverse event occurs. That mistakes occur can be attributed to many factors, including the complexity of medicine and systems that depend on memorization, as well as failures in communication and inadequate information systems.

The present model of medical training, credentialing, and continuing medical education fails to overcome self interest and does not ensure effective practice and life-long learning. Patients have no incentive to seek value. There is little available information on the comparative cost and quality of medical care and cost matters little to the patient, provided that it is covered by a third party and the co-payment is the same. Therefore, there is a need to establish a model of accountability, measured against criteria of quality medical care, with reporting to insurers and the public. Targets of efficiency, safety, and quality must be set and, as an incentive, rewards given to those who best achieve those targets. A number of techniques have been developed in industry to improve performance and these can be applied to medical care in order to address the current problems and to achieve the highest possible standards of quality and safety in medical care (41, 42).

Optimization strategies must be embedded in the management with dedicated leadership and sufficient resources; they must use accreditation as a motivator of success, and ensure that efforts to maintain quality are sustained. Factors to consider include the availability of the best possible equipment, quality and assurance systems for imaging equipment, room design, patient communication, informed consent, patient transportation, patient surveillance, all aspects of timeliness, protocols, professional communication, after-hour service, and emergency and disaster preparedness. In addition, quality of care depends on not only the performance of practitioners in the clinic, but also the contributions of workers in other areas of healthcare and the patients themselves (43). Information technology can be used to search for key performance indicators and to measure and benchmark performance and outcome.

Optimization of quality and safety requires a proactive systematic study of workflow, identification of weaknesses that could lead to sub-optimal performance, and risk assessment. In addition, a system that systematically reports medical errors, near misses, complications, and discrepancies, combined with meetings to identify causes of error may lead to the development of strategies to prevent future error. For this strategy to be successful, the error reporting process should be non-threatening and confidential. Radiology has been a pioneer in implementing such systems (44, 45).

Timeliness is a major factor in quality of care. Prompt diagnosis reduces patient anxiety, allows immediate treatment, and shortens the patient's stay in hospital. Although simplification may be complex and difficult to achieve at first, processes that are simple to learn and use save time and ultimately result in improved quality and safety. Manufacturers recognize the need to adapt to their users though examination of customer process metrics and continuous monitoring of instrument performance. As a result, corrective action can be used to improve processes for image acquisition, prevent failures, simplify maintenance, and minimize down-time. Intelligent international network infrastructures allow manufacturers to guarantee short repair times.

Utilization guidelines and diagnostic quality are difficult to implement because there are no absolute criteria. Utilization weaknesses include under use, over-use, and inappropriate use of radiologic services, all of which must be considered to prevent unnecessary escalation in healthcare costs. Nevertheless, missed diagnoses are perhaps the most significant error in the practice of radiology. Guidelines for risk management note the importance of image quality, which is dependent on factors such as equipment maintenance and selection of imaging parameters, comparison with previous examinations, missing clinical information, poor working conditions, fatigue, repeated interruption, and inadequate training (46).

Peer review combined with RIS analysis for the number of changed reports has been used to assess the quality of diagnoses. Data mining using software such as LEXIMER (39) can provide information about variations in the number of examinations ordered, findings, and recommendations. Comparison of the number of examinations ordered by individual referring physicians could be used for the purposes of utilization management or comparison of the number of findings among radiologists reports could be used as a means of quality assurance. When significant discrepancies occur without a reasonable explanation, standards of practice of individual physicians may be addressed. In addition, information on diagnostic yield of examinations could provide data for evidence based medicine and decision support for referring physicians.

Once weaknesses have been identified, diverse options to overcome or avoid them and to eliminate or reduce risk must be considered. Workflow systems need to be devised to avoid pitfalls as far as possible. They must be put in place, as a pilot if necessary, and monitored for effectiveness and to prevent "work-arounds" that void the system. After validation, the systems must be implemented throughout the organization. All this requires hard work to overcome political challenges and resistance to change.

EVIDENCE-BASED MEDICINE

Practice guidelines on imaging applications vary among different radiological societies and are, at present, developed mainly by consensus building through the convening of panels of experts. The process can be more political than scientific. Difficulties in gathering evidence on the best imaging method for a given condition are compounded by variations in instrumentation, detectors, imaging protocols, spatial resolution, post-processing, and image display. At present, imaging protocols are passed from one radiologist to another like recipes from a neighbor and are freely adapted and changed. In order to improve diagnostic accuracy and confidence, image acquisition protocols that achieve consistent image quality and reproducible diagnoses must be designed and validated through research. In addition, research to establish guidelines for effective use of imaging is needed in order to address under use, misuse and overuse.

Even when evidence on the best use of radiological examinations and procedures is available, medical practitioners do not always act on that information. At best, it takes several years for published guidelines to be adopted into routine medical practice (47). Since radiology utilization is dependent largely on the physicians who refer patients to radiology, mechanisms are needed to guide physicians in their selection of the most appropriate imaging examination in order to avoid misuse and over-use. Since self-referral for imaging examinations has been growing much faster than other uses of radiology (48, 49), it is especially important to find ways to implement evidence-based medicine in these practices.

Computer based decision support at the time of order entry has been found to improve performance in the context of delivering preventative reminders and drug doses (47). Computerized order entry systems with embedded decision support have recently been introduced for radiology and there is preliminary evidence that it does impact clinical ordering patterns (50, 51). In order to be effective, computerized order entry should be well designed and simple to use, making it easy for the clinician to do the right thing. Therefore, clinical decision support is best given rapidly and succinctly, on a single screen, before order entry is completed. The system should anticipate needs of individual patients by, for example, indicating that MRI is contraindicated for patients with electronic implants.

It is important to recognize that physicians strongly resist suggestions not to carry out an action when no alternative is offered and they will override guidelines. However, since computerized order entry requires physicians to log on, it is possible to identify physicians who do not appear to be following guidelines and to deal with them individually. Since radiologists are more likely to respond to alternative suggestions than a simple indication that a given imaging examination is not likely to yield a diagnosis, decision support can offer an alternate examination for the given clinical symptoms, when possible. Successful implementation requires monitoring to measure utilization of high cost procedures and to determine the impact of decision support. Feedback should be sought and responded to with improvements when necessary. Finally, decision support can never be static and must be updated to reflect new knowledge of evidence based medicine (47).

MOLECULAR MEDICINE

The ultimate goal of molecular medicine is to treat disease at the right time, with the right therapy at the lowest possible cost. To achieve this goal, we may envisage the use of genetic screening to identify those at risk for disease and then to detect incipient disease by screening selected high-risk groups for specific diseases. With early detection of disease, it would become theoretically possible to intervene before symptoms appear and to prevent loss of normal function. This strategy would be cost effective by lowering costs of disability and costs of treating advanced disease.

Although this goal sounds lofty and the concept of molecular medicine futuristic, it is already being applied. Genes that predict and predispose individuals to future disease have been identified and can alter patient care. For example, several genes have been identified that increase the likelihood of developing breast cancer and physicians are recommending MRI as well as mammography and clinical examination to detect cancer earlier in these women (52). Genes that are over expressed in cancers have been discovered and drugs that target the relevant gene product developed, such as trastuzumab (Herceptin) for breast cancer (53) and bevacizumab (Avastin) for rectal and colon cancer (54). Other genetic signatures have been identified that help predict response to a given therapy and will aid in the selection of therapy. In lung cancer, for example, a Phase III clinical trial demonstrated that only 8% of the patients in the trial responded to a novel drug, gefitinib (Iressa). Although the response rate was very low, it was very dramatic in the small subset of responding patients. The factor that resulted in a positive response was discovered to be a mutation in the kinase domain of the endothelial growth factor receptor, EGFR (55). Within three months of publication of that discovery, a genetic test was developed which can be used to screen patients for treatment with gefitinib (56). Though the test has not yet been validated or made commercially available, 24% of the first 100 patients tested within Partners Healthcare were found to have the mutation. Most of these patients elected to receive gefitinib, while only a small proportion of those who tested negative elected to do so.[21]

The current model for discovering the presence of a genetic variant or to detect over-expression is to biopsy tissue and perform laboratory analyses of tissue. In the future, molecular imaging methods that target gene products will be used to detect, localize, and quantify gene activity. Thus non-invasive methods will be available to monitor changes in gene activity in order to predict and monitor therapeutic effectiveness. These methods are already in use for laboratory research on disease mechanisms and pre-clinical drug development. More applications of this sort need to be developed through basic research in order to decrease both the time and the cost of drug development, which at present are major limiting factors (57). In addition, approval for molecular imaging agents needs to be facilitated by recognizing that they are different from drugs that are used for extended periods; a new set of approval criteria needs to be developed (58).

The NIH has recognized the importance of molecular imaging by founding an Imaging Probe Development Center (IPDC) to encourage the development of molecular libraries.[22] The libraries will be made up of agents that target specific proteins and can be incorporated into molecular imaging agents to gather data rapidly and non-invasively to better understand molecular interactions in biology and mechanisms of disease. The IPDC is coordinating its efforts

[21] Kucherlerpati, R. IS^{3}R Symposium, August, 2005
[22] Zerhouni, EA. IS^{3}R Symposium, August, 2005

with molecular library screening centers to help overcome some of the roadblocks in the development of molecular agents, such as probe sensitivity and specificity, toxicity studies, and advancements in imaging technologies.

Once developed, knowledge of molecular imaging agents and other contrast agents can be promulgated via the web, through sites such as the NIH Molecular Imaging and Contrast Agent Database (MICAD). In support of these activities, the NIH has committed funds to develop biomedical computing centers to integrate data, to analyze, model, and simulate systems, and to share data on human health and disease. Multi-disciplinary and interdisciplinary teams will be needed to achieve these goals. With these advances, radiology, which has a long history of multidisciplinary partnership, will be well suited to take a leading role and imaging will become a basic tool for data acquisition that has the potential to transform medicine.

Both molecular imaging agents and functional imaging techniques show promise as surrogate end-points for clinical trials, that is, early predictors of response to therapy. Recognizing that a patient has responded to therapy is slow or difficult for many diseases. For cancer, determining the effectiveness of a new drug using the clinical endpoint of extended survival requires clinical trials that take years and need large numbers of patients. Even the time to determine response through tumor shrinkage takes months. However, early changes in the uptake of 18F-fluorodeoxyglucose, measured with PET, has been shown to be a predictor of survival for some cancers (59). Changes in hemodynamic parameters, measured by dynamic contrast imaging can be detected within hours or days after the initiation of antiangiogenic or antivascular therapy and are predictors of tumor shrinkage (60). Differences in hemodynamic parameters demonstrated by imaging among patients with cervical cancer have been shown to correlate with survival (60). Other biomarkers of cancer detectable with imaging include hypoxia, cell proliferation, and apoptosis.

Imaging biomarkers for another major killer, cardiovascular disease, are also being developed. FDG-PET has been shown to detect inflamed atherosclerotic plaque (61). Many neurological diseases are difficult to detect early and measures of the rate of disease progression are slow and imprecise. BOLD fMRI and molecular imaging with PET may be useful as surrogate markers for both drug development and therapy in these conditions.

EDUCATION AND RESEARCH TRAINING

For radiology to play a significant role in the development and application of molecular medicine, radiologists must have an understanding of cell biology, be involved in multidisciplinary research teams, collaborate with industry to overcome regulatory hurdles, and organize clinical trials. Clinical research needs to be rejuvenated though the creation of new academic centers dedicated to translational research and positioned to deal with the complexity of models and regulations while providing a sheltered environment in which young physicians can become involved in research. These centers will be integrated via the Internet though the National Electronic Clinical Trials and Research (NECTAR) information system, which provides end-to-end clinical research data management tools and facilitates effective business practice, enhanced data sharing, and rapid translation and diffusion of research results.

Although support for radiology research has nearly quadrupled in the decade 1995-2005, research programs are unevenly distributed in the United States. Of the 160 medical schools, half have no radiology research support, while 50% of grant money went to only 7 departments. There are very few clinical fellows in radiology compared to other medical specialties, especially surgery, where many departments require two years of research as part of their residency training.[23] Institutional leadership and radiology department commitment are needed to increase research

[23] Baum, S. IS³R Symposium, August, 2005

training, develop research themes, and support those involved in the challenging and time consuming process of translation of basic research into clinical practice. Radiology departments should hire more researchers with Ph.D.s in allied fields to develop multidisciplinary teams. Failure to achieve these goals will result in ownership of advances in imaging by other medical specialties and relegate radiology departments to becoming trade schools. Research support is available both in Europe through the European Institute for Biomedical Imaging Research (EIBIR) and in the United States through the National Institute of Biomedical Imaging and Bioengineering (NIBIB).

REFERENCES

1. Bhargavan M, Sunshine JH. Utilization of radiology services in the United States: levels and trends in modalities, regions, and populations. Radiology 2005; 234:824-832.

2. Levin DC, Spettell CM, Rao VM, Sunshine J, Bansal S, Bushee GR. Impact of MR imaging on nationwide health care costs and comparison with other imaging procedures. AJR Am J Roentgenol 1998; 170:557-560.

3. Levin DC, Parker L, Intenzo CM, Sunshine JH. Recent rapid increase in utilization of radionuclide myocardial perfusion imaging and related procedures: 1996-1998 practice patterns. Radiology 2002; 222:144-148.

4. Livstone BJ, Parker L, Levin DC. Trends in the utilization of MR angiography and body MR imaging in the US Medicare population: 1993-1998. Radiology 2002; 222:615-618.

5. Mitchell DG, Parker L, Sunshine JH, Levin DC. Body MR imaging and CT volume: variations and trends based on an analysis of Medicare and fee-for-service health insurance databases. AJR Am J Roentgenol 2002; 179:27-31.

6. Maitino AJ, Levin DC, Parker L, Rao VM, Sunshine JH. Nationwide trends in rates of utilization of noninvasive diagnostic imaging among the Medicare population between 1993 and 1999. Radiology 2003; 227:113-117.

7. Henley MB, Mann FA, Holt S, Marotta J. Trends in case-mix-adjusted use of radiology resources at an urban level 1 trauma center. AJR Am J Roentgenol 2001; 176:851-854.

8. Wittram C, Meehan MJ, Halpern EF, Shepard JA, McLoud TC, Thrall JH. Trends in thoracic radiology over a decade at a large academic medical center. J Thorac Imaging 2004; 19:164-170.

9. Sunshine JH, Mabry MR, Bansal S. The volume and cost of radiologic services in the United States in 1990. AJR Am J Roentgenol 1991; 157:609-613.

10. Brennan TA, Hebert LE, Laird NM, et al. Hospital characteristics associated with adverse events and substandard care. JAMA 1991; 265:3265-3269

11. Thomas EJ, Orav EJ, Brennan TA. Hospital ownership and preventable adverse events. Int J Health Serv 2000; 30:745-761.

12. Kohn L, Corrigan J, Donaldson M, eds. To Err is Human: Building a Safer Health System. Washington DC: Committee on Quality of Health Care in America, Institute of Medicine. National Academy Press, 2000.

13. Bryan S, Weatherburn G, Watkins J, et al. Radiology report times: impact of picture archiving and communication systems. AJR Am J Roentgenol 1998; 170:1153-1159.

14. Reiner BI, Siegel EL, Hooper FJ, Pomerantz S, Dahlke A, Rallis D. Radiologists' productivity in the interpretation of CT scans: a comparison of PACS with conventional film. AJR Am J Roentgenol 2001; 176.

15. Bhargavan M, Sunshine JH. Workload of radiologists in the United States in 2002-2003 and trends since 1991-1992. Radiology 2005; 236:920-931.

16. Hogan C, Sunshine JH. Financial ratios in diagnostic radiology practices: variability and trends. Radiology 2004; 230:774-782.

17. McCall I. Benchmarking Radiological Services in Europe. In: European Association of Radiologists, 2005; *http://www.ear-online.org/download/Benchmarking_radiological_services_in_Europe.pdf*

18. Reiner BI, Siegel EL, Hooper FJ. Accuracy of interpretation of CT scans: comparing PACS monitor displays and hard-copy images. AJR Am J Roentgenol 2002; 179.

19. Larson DB, Cypel YS, Forman HP, Sunshine JH. A comprehensive portrait of teleradiology in radiology practices: results from the American College of Radiology's 1999 Survey. AJR Am J Roentgenol 2005; 185:24-35.

20 Wong W, Roubal I, Jackson D, Paik W, Wong V. Outsourced teleradiology imaging services: An analysis of discordant interpretation in 124,870 cases. J Am Coll Radiol 2005; 2:478-484.

21. ACR Task Force on International Teleradiology. J Am Coll Radiol 2005; 2:121-125.

22. Freer TW, Ulissey MJ. Screening mammography with computer-aided detection: prospective study of 12,860 patients in a community breast center. Radiology 2001; 220:781-786.

23. Cupples TE, Cunningham JE, Reynolds JC. Impact of computer-aided detection in a regional screening mammography program. AJR Am J Roentgenol 2005; 185:944-950.

24. Uchiyama Y, Katsuragawa S, Abe H, et al. Quantitative computerized analysis of diffuse lung disease in high-resolution computed tomography. Med Phys 2003; 30:2440-2454.

25. Li Q, Sone S, Doi K. Selective enhancement filters for nodules, vessels, and airway walls in two- and three-dimensional CT scans. Med Phys 2003; 30:2040-2051.

26. Arimura H, Li Q, Korogi Y, et al. Automated computerized scheme for detection of unruptured intracranial aneurysms in three-dimensional magnetic resonance angiography. Acad Radiol 2004; 11:1093-1104.

27. Suzuki K, Armato SG, 3rd, Li F, Sone S, Doi K. Massive training artificial neural network (MTANN) for reduction of false positives in computerized detection of lung nodules in low-dose computed tomography. Med Phys 2003; 30:1602-1617.

28. Li Q, Li F, Shiraishi J, Katsuragawa S, Sone S, Doi K. Investigation of new psychophysical measures for evaluation of similar images on thoracic computed tomography for distinction between benign and malignant nodules. Med Phys 2003; 30:2584-2593.

29. Li F, Aoyama M, Shiraishi J, et al. Radiologists' performance for differentiating benign from malignant lung nodules on high-resolution CT using computer-estimated likelihood of malignancy. AJR Am J Roentgenol 2004; 183:1209-1215.

30. Mehta A, McLoud TC. Voice recognition. J Thorac Imaging 2003; 18:178-182.

31. Talton D. Perspectives on speech recognition technology. Radiol Manage 2005; 27:38-40.

32. Holman BL, Aliabadi P, Silverman SG, Weissman BN, Rudolph LE, Fener EF. Medical impact of unedited preliminary radiology reports. Radiology 1994; 191:519-521.

33. Bramson RT, Bramson RA. Overcoming obstacles to work-changing technology such as PACS and voice recognition. AJR Am J Roentgenol 2005; 184:1727-1730.

34. Reiner B, Siegel E, Protopapas Z, Hooper F, Ghebrekidan H, Scanlon M. Impact of filmless radiology on frequency of clinician consultations with radiologists. AJR Am J Roentgenol 1999; 173:1169-1172.

35. Khorasani R, Bates DW, Teeger S, Rothschild JM, Adams DF, Seltzer SE. Is terminology used effectively to convey diagnostic certainty in radiology reports? Acad Radiol 2003; 10:685-688.

36. Kolata G. Sick and scared, and waiting, waiting, waiting. In: New York Times. New York, 2005; August 20, A1.

37. Berlin L. Communicating findings of radiologic examinations: whither goest the radiologist's duty? AJR Am J Roentgenol 2002; 178:809-815.

38. ACR practice guideline for communication of diagnostic imaging findings. In: American College of Radiology, 2005; *http://www.acr.org/s_acr/bin.asp?TrackID=&SID=1&DID=12196&CID=541&VID=2&DOC=File.PDF*

39. Dreyer KJ, Kalra MK, Maher MM, et al. Application of recently developed computer algorithm for automatic classification of unstructured radiology reports: validation study. Radiology 2005; 234:323-329.

40. Walker J, Pan E, Johnston D, Adler-Milstein J, Bates DW, Middleton B. The value of health care information exchange and interoperability. Health Affairs (Millwood) 2005; January 19:10-18.

41. Thrall JH. Quality and safety revolution in health care. Radiology 2004; 233:3-6.

42. Hillman B, Amis E, Neiman H. The Future Quality and Safety of Medical Imaging: Proceedings of the Third Annual ACR FORUM. J Am Coll Radiol 2004; 1:33-39.

43. Donabedian A. The quality of care. How can it be assessed? JAMA 1988; 260:1743-1748.

44. Melvin C, Bodley R, Booth A, Meagher T, Record C, Savage P. Managing errors in radiology: a working model. Clin Radiol 2004; 59:841-845.

45. Wheeler PS. Risk prevention, quality assurance, and the missed diagnosis conference. Radiology 1982; 145:227-228.

46. Cooper MA. Optical biosensors in drug discovery. Nat Rev Drug Discov 2002; 1:515-528.

47. Bates DW, Kuperman GJ, Wang S, et al. Ten commandments for effective clinical decision support: making the practice of evidence-based medicine a reality. J Am Med Inform Assoc 2003; gg0dddf10:523-530.

48. Levin DC, Rao VM. Turf wars in radiology: possible remedies for self-referral that could be taken by Federal or State Governments and payers. J Am Coll Radiol 2004; 1:806-810.

49. Levin DC, Rao VM. Turf wars in radiology: Other causes of overutilization and what can be done about it. J Am Coll Radiol 2004; 1:317-321.

50. Sanders DL, Miller RA. The effects on clinician ordering patterns of a computerized decision support system for neuroradiology imaging studies. Proc AMIA Symp 2001:583-587.

51. Rosenthal D, Weiburg J, Schultz T, et al. Radiology order entry with decision support: Initial clinical experience.(“J Am Coll Radiol, in press”).

52. Kriege M, Brekelmans CT, Boetes C, et al. Efficacy of MRI and mammography for breast-cancer screening in women with a familial or genetic predisposition. N Engl J Med 2004; 351:427-437.

53. De Laurentiis M, Cancello G, Zinno L, et al. Targeting HER2 as a therapeutic strategy for breast cancer: a paradigmatic shift of drug development in oncology. Ann Oncol 2005; 16 Suppl 4:iv7-iv13.

54. Willett CG, Boucher Y, Di Tomaso E, et al. Direct evidence that the VEGF-specific antibody bevacizumab has antivascular effects in human rectal cancer. Nat Med 2004; 10:145-147.

55. Lynch TJ, Bell DW, Sordella R, et al. Activating mutations in the epidermal growth factor receptor underlying responsiveness of non-small-cell lung cancer to gefitinib. N Engl J Med 2004; 350: 2129-39

56. Couzin J. Cancer Sharpshooters Rely on DNA Tests for a Better Aim. Science, 2004; 305:1222-1223.

57. DiMasi JA, Hansen RW, Grabowski HG. The price of innovation: new estimates of drug development costs. J Health Econ 2003; 22:151-185.

58. Henderson J, Alexander B, Smith J. The Food and Drug Administration and Molecular Imaging Agents: Potential Challenges and Opportunities. J Am Coll Radiol 2005; 2:833-840.

59. Weber WA. Use of PET for monitoring cancer therapy and for predicting outcome. J Nucl Med 2005; 983-995.

60. Miller JC, Pien HH, Sahani D, Sorensen AG, Thrall JH. Imaging angiogenesis: applications and potential for drug development. J Natl Cancer Inst 2005; 97:172-187.

61. Davies JR, Rudd JF, Fryer TD, Weissberg PL. Targeting the vulnerable plaque: the evolving role of nuclear imaging. J Nucl Cardiol 2005; 12:234-246.

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