The Latest in Oncology Management: Diagnostic Nuclear Medicine and Molecular Imaging

For Health Plans, Medical Management Organizations and TPAs

Executive Summary

Despite a significant number of new cancer diagnoses and deaths each year, the relative survival rate for all cancers has been increasing steadily for the past 2 decades, reflecting improvements in detection and treatment.

Nuclear medicine and molecular imaging provide information about both body structure and function, allowing physicians to gather medical information that would otherwise be unavailable, require surgery, or necessitate more expensive diagnostic tests. These studies are quite useful for the diagnosis, staging, and follow-up of cancer patients. Continually evolving technologies have allowed more widespread application of nuclear and molecular imaging, and one of the more recent advancements is the development of hybrid imaging modalities.

The American Cancer Society (ACS) estimates that about 1.6 million new cancer cases will be diagnosed in 2011, with almost 600,000 Americans expected to die of cancer. Cancer is the second most common cause of death in the United States, exceeded only by heart disease.

Independent medical review facilitates the evaluation of medical need for nuclear medicine and molecular imaging in the diagnosis and management of cancer, which requires reviewers who have in-depth training and understanding of not only these technologies, but also the clinical course and findings of cancer and the available treatment options. The process also avoids issues such as conflicts of interest, not having the appropriate specialists to review cases, or having the same physician who initially denied a claim also review an appeal.

Introduction

The American Cancer Society (ACS) estimates that about 1.6 million new cancer cases will be diagnosed in 2011, with almost 600,000 Americans expected to die of cancer. Cancer is the second most common cause of death in the United States, exceeded only by heart disease.

Despite these sobering statistics, the death rate for cancer has generally been declining steadily since 1991, with 5-year survival rates increasing as well. These trends reflect improvement in early detection and treatment. Nuclear medicine and molecular imaging have become part of the standard of care for many types of cancer. They are functional imaging technologies that involve the use of radioactive isotopes in the diagnosis and treatment of disease.

The images these studies provide allow functional visualization of virtually any area of the body. The technologies are constantly evolving and continually providing greater insight into the functioning of the body in various disease states, thereby providing important clues regarding treatment as well.

Nuclear Medicine vs. Traditional Anatomic Imaging

Nuclear medicine is a subspecialty of radiology that provides detailed images of different organ systems at the molecular and cellular level, allowing physicians to gather information predominantly about function. It differs from the traditional anatomic imaging technologies such as computed tomography (CT) or magnetic resonance imaging (MRI) because it determines the presence of disease on the basis of metabolic changes rather than changes in organ structure. Nuclear medicine imaging procedures often identify abnormalities very early in the progress of a disease, long before many medical problems can be detected with other diagnostic tests.

While therapeutic nuclear medicine involves large amounts of radioactive materials, diagnostic nuclear medicine uses small amounts of radioactive materials (radiopharmaceuticals or tracers specifically targeted to a certain organ function) given by injection, swallowing, or inhalation. Radiopharmaceuticals emit small amounts of radiation as they move through the body, making it possible to visualize specific disease and treatment processes. The amount of radiopharmaceutical used is carefully selected to provide the least amount of radiation exposure to the patients, but at the same time ensure an accurate test. Specialized cameras (e.g., PET or SPECT/gamma camera) detect the emitted radiation, and the resulting images reflect the function, rather than the structure, of the organ system or metabolic process being evaluated. Nuclear medicine differs from an x-ray, ultrasound, and other traditional diagnostic tests because it determines the presence of disease based on biological changes rather than changes in anatomy and it can reveal abnormalities that static forms of anatomic imaging cannot detect.

Nuclear imaging methods and anatomic imaging methods play complementary roles in oncologic medicine by providing functional images vs. structural images.

Nuclear medicine encompasses molecular imaging, which is a highly targeted version of nuclear medicine that illustrates function on a deeper and even more specific molecular level. Molecular imaging allows physicians to see how the body is functioning and to measure its chemical and biological processes. It provides information that other imaging technologies cannot provide or that would otherwise require more invasive procedures such as biopsy or surgery. Molecular imaging is also able to identify disease in its earliest stages and determine the exact location of a tumor often before symptoms occur or abnormalities can be detected with other diagnostic tests, signaling a shifting paradigm from treating late disease to pinpointing and diagnosing disease sooner.

Nuclear imaging methods and anatomic imaging methods play complementary roles in oncologic medicine by providing functional images vs. structural images. With nuclear medicine, the resolution of structures of the body will be quite poor compared to anatomic imaging techniques such as CT and magnetic resonance imaging MRI. Similarly, anatomic imaging typically does not provide information regarding organ function. Using hybrid technology (PET/CT, SPECT/CT), nuclear medicine images can be superimposed on CT or MRI images to produce hybrid studies in which the information from the two different modalities are correlated together, allowing precise anatomic localization of functional abnormalities.

Nuclear Medicine and Molecular Imaging Techniques: Clarifying Terminology

Scintigraphy

Scintigraphy is a two-dimensional (2D) "standard" nuclear medicine procedure, e.g., bone scintigraphy ("bone scan") that is routinely done in prostate cancer patients to look for bone metastases.

Single-Photon Emission Computed Tomography (SPECT)

SPECT is a three-dimensional (3D) technique applicable to many standard scintigraphic studies, which increases resolution of the exam (the analogy in anatomic imaging would be the standard chest x-ray, which is 2D, vs. the chest CT scan, which is 3D). Note then that for oncology imaging, many of the tests can be done as 2D (scintigraphy) or in 3D as well (SPECT). As a general rule, it is well documented that doing SPECT in these cases yields a much superior result and is the typical the default.

Positron Emission Tomography (PET)

PET is a specific type of molecular imaging; the most common active molecule used for imaging is FDG, which is an analog of glucose, but there are several other active molecules available or in development.

Hybrid Techniques

Correlative imaging (i.e., comparing or combining images obtained from multiple studies) has been used in clinical practice for many years, particularly for nuclear medicine studies, which by themselves lack detailed anatomical information. Technical limitations of this practice included those relating to the different geometries of the imaging equipment, different patient positioning, and displacement of mobile structures between studies. These issues eventually led to the development of hybrid devices, such as PET/CT, SPECT/CT, and PET/MRI units most recently, enabling precise correlation of functional/metabolic abnormalities with anatomic structure.

The Role of Nuclear Medicine and Molecular Imaging in Cancer Management

Greater scientific understanding of the biology of cancer has broadened the role of nuclear medicine and molecular imaging in cancer management in recent years. Nuclear medicine and molecular imaging play a critical role throughout every phase, including:

- Diagnosis and staging
- Treatment planning
- Monitoring response to therapy
- Monitoring for recurrent/residual disease

As tools for diagnosing and staging a patient, nuclear medicine and molecular imaging can detect disease that would go undetected by other imaging modalities Staging is necessary once cancer is detected in order to determine the extent or severity of disease, including degree of spread throughout the body. Nuclear medicine and molecular imaging studies often result in changed staging, upstaging or downstaging the initial staging that was done by routine methods (i.e., clinically and with anatomic imaging such as CT and MRI); altered staging is critical, of course, in that it typically results in altered management.

In planning treatment, the most effective therapy is selected based on the unique biologic characteristics of the patient and the molecular properties of the tumor or other disease that nuclear medicine and molecular imaging reveal. Accurate staging is also critical in treatment planning.

The patient's response to ongoing therapy is best done with functional imaging rather than anatomic imaging, as typically anatomic changes will lag behind functional changes, or anatomic changes can even be misleading. This is critical because it allows treatment to be altered midcourse, if necessary, as opposed to waiting for structural changes revealed by anatomic imaging much further down the line, while completing a course of therapy that may not be particularly effective.

Finally, nuclear imaging is quite useful for detection of residual disease or surveillance for recurrence. A classic use for nuclear imaging is to evaluate focal soft tissue in a tumor bed after treatment as demonstrated by CT or MRI, which are unable to differentiate scar tissue from residual tumor, unlike PET imaging.

Guidelines for Using Nuclear Medicine and Molecular Imaging in Patients with Cancer

There are a number of sources for practice guidelines, including the Centers for Medicare & Medicaid Services National Coverage Determinations (CMS NCD) Manual, as well as the guidelines set forth by the National Comprehensive Cancer Network (NCCN). In most cases, these two sources allow clinicians to quickly and easily assess the appropriateness of a given study in individual patients. The CMS NCD Manual is particularly useful for PET imaging standards, and the NCCN guidelines detail the work-up and surveillance for all of the most common cancers. The SNM, which recently announced a collaboration with the NCCN to advance research for cancer imaging and therapies, also provides useful guidelines for oncology. Please see Table 1 for a sample of these practice guidelines for the use of PET and PET/CT in the cancer types covered by Medicare.

Table 1. Summary of Practice Guidelines for PET and PET/CT in Common Cancers

Type of Cancer	Practice Guidelines
Head and Neck	▶ Detection of occult primary tumors in patients presenting with metastatic disease ▶ Initial staging, including detection of cervical lymph node metastases in the clinically node-negative neck, and detection of distant metastases in patients with locally advanced disease ▶ Detection of residual or recurrent disease
Thyroid	▶ Detection of residual or recurrent thyroid cancer of follicular cell origin when serum thyroglobulin is elevated and radioiodine scan is negative
Breast	▶ Detection of metastatic or recurrent breast cancer in those patients clinically suspected of metastases or recurrence
Lung	▶ Characterization of indeterminate pulmonary nodules at least 8-10 mm in diameter ▶ Initial staging in patients with non-small cell lung cancer (stages I-IV) ▶ Delineation of gross-tumor volume (GTC) in patients receiving radiation therapy
Esophagus	▶ Initial staging of stage I-III cancer ▶ Restaging after neoadjuvant chemoradiation therapy ▶ Delineation of gross-tumor volume (GTC) in patients receiving radiation therapy
Colorectal	▶ Preoperative evaluation of patients with potentially resectable hepatic or other metastases ▶ Determining location of tumors if rising carcinoembryonic antigen (CEA) level suggests recurrence
Cervical	▶ Initial treatment planning assistance, including determination of nodal status and systemic spread ▶ Detection of residual or recurrent disease
Melanoma	▶ Detection of extranodal metastases in stage II-III disease ▶ Evaluation of extent of recurrent disease
Lymphoma	▶ Routine pre-treatment staging of patients with Hodgkin's disease and non-Hodgkin's lymphoma (especially diffuse large B-cell lymphoma), including evaluation of bone marrow involvement ▶ Routine re-staging after completion of chemotherapy and after radiation therapy

The Role of External Independent Medical Review for Diagnostic Nuclear Medicine and Molecular Imaging in Oncology

Practice guidelines are continually changing to reflect the advances in imaging technologies, which often complicates the process of establishing evidence-based criteria for practice guidelines and reimbursement for new procedures and treatments. An independent medical review, which is normally used by healthcare payers, looks at whether or not a specific procedure was medically necessary.

The specialty match that an independent review organization (IRO) provides is especially important for nuclear medicine and molecular imaging since these areas of medicine require a high degree of specialized training. The board-certified physician specialists who work with IROs keep up-to-date with the latest medical research literature and with the latest standard of care. Physicians who review cases for IROs stay on top of continually evolving technology and treatments as they are studied more extensively and potentially accepted into clinical guidelines.

Independent medical reviews also avoid conflicts of interest, not having the appropriate specialists to review cases, or having the same physician who initially denied a claim also review an appeal. Independent medical review facilitates effective treatment of patients with cancer, which requires an in-depth understanding of the diagnostic imaging technologies so that disease management can be individualized for each patient.

Conclusions

Diagnostic imaging technologies have become increasingly sophisticated in recent years. Nuclear medicine and molecular imaging allow physicians to assess function, that is, what is happening in the body at cellular and molecular levels, and in combination with traditional anatomic imaging such as CT and MRI, provide precise localization of functional abnormalities. Thus, they provide information that is unattainable with more traditional imaging technologies, or that would otherwise require more invasive procedures such as biopsy or surgery. These advances in diagnostic imaging help optimize the disease management process and increase the chances of survival.

An IRO can provide ready access to specialists, which healthcare plans may lack internally, allowing for timely determination of whether the requested treatment falls under medical necessity guidelines. Independent medical reviews provide unbiased evaluation of medical need for nuclear medicine and molecular imaging in cancer diagnosis and management.

Sources

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