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ABSTRACT: Imaging plays an important role in the management of cancer patients, and in screening of asymptomatic individuals for early detection of cancer. This paper will review the clinical applications of oncologic imaging in the diagnosis, staging and follow-up in cancer patients and screening for cancer.

INTRODUCTION

The year is 1970, you have a patient in your clinic with the diagnosis of colon carcinoma that just finished his chemotherapy a few months ago and is complaining of generalized abdominal discomfort and elevated liver function tests. He comes to you because he wants to know whether he has, (a) recurrent disease, (b) metastatic disease to the liver or lungs. This was a very frustrating experience for treating physicians and radiologists. We had little to offer at that time. CT and ultrasound were just being introduced to clinical practice. MRI was unheard of, and at that time nuclear medicine was not available in Lebanon. PET and PET/CT did not exist. We had to rely on plain X-rays and in difficult cases tomography, to try and define lung masses. Lymphangiography was of help in staging patients with Hodgkin’s disease, and cerebral angiography was used to diagnose space occupying lesions in the brain. Skeletal series was used to look for bone metastases. It would have been a very frustrating experience to try and stage or follow-up a patient with cancer.

During the last three decades of the twentieth century and continuing into the beginning of the twenty-first century, there have been remarkable advances in the field of medical imaging that greatly impacted on all aspects of medicine, including oncology.

In recent years, the care for cancer patients is no longer in the hands of the oncologist alone, it has become a multidisciplinary approach that requires the input of the oncologist, the surgeon, the pathologist, the radiation oncologist and the radiologist. Imaging is now a very essential part in the diagnosis, staging and follow-up of patients with cancer, and more recently is playing an important role in better defining the fields of radiation therapy. There are very few malignancies that do not require some imaging study or studies in their management.

The advances in imaging technologies that include exquisite anatomical imaging with Multi-detector CT, MRI and ultrasound have provided us with road maps for planning surgery and radiation therapy. The addition of “functional” and “biologic” imaging is providing us with new methodology to evaluate tumor viability, extent and biologic behavior. The merging of function and anatomy in PET/CT and SPECT/CT has provided us with a new outlook at the behavior of tumors.

The role of imaging however is not just limited to the diagnosis, staging and follow-up of cancer, imaging plays an important role in screening asymptomatic individuals for cancer. This article will discuss the role of imaging in screening, diagnosis, staging and the follow-up of cancer patients.

SCREENING

Mammography is the best example of an imaging screening modality that had a strong impact on the management of breast cancer. Whereas in the past tumors were detected when they were of large size, with the increased use of screening mammography breast tumors are usually detected when of much smaller size (< 2 cm) (Fig. 1) [1]. There is a smaller chance of axillary lymph node involvement, thus resulting in breast conserving surgery and less axillary lymph node dissection. In high risk women in whom mammography may not be helpful i.e. those with dense breasts, alternative screening modalities such as ultrasound (US) and contrast enhanced breast magnetic resonance imaging (MRI) are being employed. Several studies performed in the last few years have shown contrast enhanced MRI to be more sensitive than mammography or US in patients at high risk of developing breast cancer. MRI had a sensitivity of 71%-100%, mammography 16%-40% and US 16%-33% [2-5]. Despite its high sensitivity MRI is still not recommended for general screening because of its lack of availability to the general public and is more expensive than mammography, but is of value in high risk individuals and in evaluation for multicentric and multifocal disease. The role of ultrasound as a screening tool remains questionable, although US plays a very important role in evaluating questionable mam-
mographic findings and in patients with dense breast parenchyma on mammography. Nothing however replaces the role of mammography in detecting microcalcifications.

Screening for lung cancer however remains a topic of much uncertainty. Everyone agrees that chest X-rays can miss a large number of early stage 1 cancers. The feasibility of low dose CT for screening for lung cancer is still a strongly debated question. Several studies have demonstrated that screening will detect more stage 1 cancers (Fig. 2) [6-10], however, this has not led to a decrease in mortality [10]. But some like Bach et al. [10] feel that it has led to an increase in invasive procedures and surgery. On the other hand, Henschke et al. in an article published in the New England Journal of Medicine [11] conclude that “…annual spiral CT screening can detect lung cancer that is curable”. The debate continues and there are studies by the American College of Radiology and the National Cancer Institute to evaluate the role of “Lung CT” as a screening tool for detection of lung cancer and its impact on survival.

We agree however with Dr. Henschke’s position that “it is reasonable for a smoker or former smoker to consider screening and it is reasonable for them to get a screening CT at a center with experience in this area”.

Optical colonoscopy essentially replaced the use of the barium enema as a screening method for colonic polyps and malignancies. Virtual colonoscopy, a noninvasive technique developed as a result in the recent improvements in CT technology, has emerged as a new alternative to colonoscopy for screening for colonic premalignant
lesions and colon carcinoma (Fig. 3). A meta-analysis of studies regarding the sensitivity and specificity of virtual colonoscopy [12] showed that the sensitivity of CT colonography was heterogeneous but improved as polyp size increased: 48% for detection of polyps < 6 mm, 70% for polyps 6 to 9 mm, and 85% for polyps > 9 mm. Specificity, however, was homogenous (92% for detection of polyps < 6 mm, 93% for polyps 6 to 9 mm, and 97% for polyps > 9 mm). Virtual colonoscopy is better tolerated than optical colonoscopy, the drawback is the radiation exposure and the fact that the patient will eventually require an optical colonoscopy for biopsy of suspicious polyps. One of its advantages however, is that it can detect extra colonic disease that can involve the rest of the abdominal organs including unsuspected malignancies.

Research is currently being performed to evaluate MR colonography as a colorectal screening method. Cost and accuracy will be some of the issues MR colonography has to face when competing with CT virtual colonoscopy, the advantage being the lack of radiation exposure.

**DIAGNOSIS AND STAGING**

In a multidisciplinary approach to cancer, the role of the radiologist is not only to help in confirming the presence of a cancer, but also to provide an accurate pretreatment staging of the tumor, to monitor the response to treatment, and to provide follow-up in cases of curative treatment, whether surgery, radiation therapy or chemotherapy.

Because of major advances in cancer treatment and the earlier detection of cancer because of more screening tests for more tumors, the information provided by imaging nowadays has to provide accurate documentation of the morphology and spread of the tumor, and regarding its biology and function when possible.

The role of imaging in the diagnosis of cancer is well established. The classic findings of microcalcifications or a spiculated lesion by mammography are essentially diagnostic of breast carcinoma. An apple core lesion on barium enema (Fig. 4) or a CT of the colon raises the possibility of colon carcinoma. A brain mass with necrosis and surrounding edema is consistent with a malignant glioma (Fig. 5). And there are many examples that one can consider where imaging may be the first tool to diagnose a malignant process. Yet this initial imaging evaluation allows us, radiologists, to provide a differential diagnosis of the lesion based on its imaging findings and characteristics. For us to establish a pathologic diagnosis prior to definitive therapy, other procedures are required and imaging here plays an important role in the planning of the necessary intervention. One of the most important diagnostic steps is image guided biopsy, either a fine needle aspiration (FNA) or a core biopsy. This can be done under CT or US guidance, or even in some cases using MR guidance. An FNA of a lung mass can be done with CT guidance.
(Fig. 6) while a biopsy of a thyroid nodule may be US guided, and so would a prostate biopsy. These techniques in the hands of experienced radiologists have a high sensitivity for detection of malignancy of about 75%-98% [14-16]. Some of the complications include bleeding, and hemoptysis and pneumothrax in case of lung biopsies. On-site immediate evaluation of FNA specimens can be beneficial in determining the adequacy of the aspirate and in providing accurate preliminary diagnoses of the specimens, thus allowing for rapid clinical decision.

Endoscopic ultrasound (EUS) is also emerging as a new technology that is proving useful in guiding FNA from tumors and/or adjacent suspected lymph nodes (Fig. 7). The accuracy of EUS for the T (tumor) staging of rectal carcinoma ranges from 80-95% compared with CT (65-75%) and MR imaging (75-85%) [18]. The sensitivity of CT or US guided FNA and EUS guided FNA for detecting pancreatic malignancy was 62% and 84%, respectively. A comparison of the accuracy for CT/US-FNA and EUS-FNA was not statistically significant ($p = .074$) according to Horwhat et al. [19]. One of the

![Figure 5](image5.png)  
**Figure 5**  
Contrast enhanced CT examination of the brain shows a peripherally enhancing lobulated mass in the left hemisphere, crossing the midline (arrows) with surrounding edema and mild mid line shift (arrow heads). The findings are typical of a glioblastoma multiformis (GBM).

![Figure 6](image6.png)  
**Figure 6**  
With the patient in the prone position the biopsy needle can be seen in the left upper lobe mass in this CT guided FNA of a lung tumor.

![Figure 7](image7.png)  
**Figure 7.**  
a. Endoscopic ultrasound examination of the pancreas demonstrates a mass in the head of the pancreas as a lobulated hypoechoic lesion; in addition it clearly demonstrates the dilated common bile duct (CBD) and the relationship of the mass to the superior mesenteric vein (SMV)  
b. T4N1 rectal carcinoma. Endoscopic ultrasound shows a mass involving all the layers of the rectal wall, extending to adjacent soft tissues (arrow heads) and an enlarged malignant looking adjacent lymph node (arrow).
The important role of imaging in confirming the presence of cancer is overshadowed by a more important role that it plays in staging disease. The treatment of cancer patients, particularly those with solid tumors, is dependent on the stage of the disease, the presence or absence of distant metastasis or lymph node involvement. Short of surgical exploration, imaging is the only way this information can be made available to help in planning treatment protocols.

CT plays a very important role in tumor staging. It has set the standards by which preoperative staging of cancers such as lung, colon and kidney is performed. CT plays an essential role in not only demonstrating the local extent of the tumor but also adds invaluable information regarding distant metastasis to organs such as liver and brain (Fig. 8). It is a reliable method to evaluate the status of lymph nodes in both solid tumors as well as hematological malignancies. It is essential in evaluating the lungs for the presence of metastasis from gastrointestinal and genitourinary malignancies as well as from bone and soft tissue sarcomas.

In the last two decades contrast enhanced MRI has replaced CT as the method of choice for evaluating patients with primary CNS tumors and in evaluating the brain for the presence of brain metastasis from distant tumors such as lung and breast cancers (Fig. 9). More recently MRI is playing an important role in evaluating patients with gynecologic malignancies. It plays a very important role in determining myometrial invasion and extension of tumor, and is useful in lymph node evaluation [20-21]. MRI was shown to be more specific and accurate than US and Doppler for differentiating malignant from benign adnexal masses [22].

MRI is gaining increased use in breast carcinoma. In addition to its use as a screening modality in a certain population of high-risk patients, it is becoming a very promising technique in evaluating patients with diagnosed or suspected breast carcinoma because of its ability to detect multifocal and multicentric disease, it can detect occult cancer in the contralateral breast thus resulting in a change of the initial management plan, without increasing the number of biopsies [23].

Because different imaging modalities have different soft tissue contrast properties, we had to rely on the use of several imaging modalities in order to evaluate the tumor extent for accurate staging. CT was used for lung and liver metastasis, bone scintigraphy for bone metaста-
sis, and MRI for brain metastasis. The introduction of positron emission tomography (PET) and more recently PET/CT fusion imaging can provide us with a possible alternative solution, where one imaging modality can provide accurate evaluation of tumor extent and allow proper staging with a one-stop-shop examination.

PET is a “functional” imaging modality that uses radioactive tracers, the most commonly used agent is F-18 deoxy-glucose (FDG). FDG is an analogue of glucose and its distribution in the body reflects glucose metabolism. Tumor cells have increased glucose metabolism and increased glucose transporter proteins (GLUT-1) in their cell membranes resulting in increased uptake of FDG. Total body scans can be performed and reformatted in multiple planes allowing total body evaluation that includes the primary tumor and any metastatic deposits.

Since its introduction in the mid 1990s PET has been used to differentiate benign from malignant disease. A meta-analysis of 40 studies totaling 1474 lung masses reported a sensitivity and specificity of PET for detection of malignant lesions to be 96.8% and 77.8% respectively [24]. CT was the method of choice for staging patients with cancer. However, several studies showed that CT has limited sensitivity (64%) and specificity (62%) in staging nodal involvement in patients with lung cancer [25]. Thus other invasive procedures like mediastinoscopy and at times thoracotomy are needed for a definitive diagnosis. FDG-PET has been proven to be far superior to CT in the staging of lung cancer, particularly non small cell lung carcinoma (NSCLC). In a study of 102 patients with NSCLC PET had a sensitivity and specificity of 91% and 86% in detecting mediastinal lymph node metastasis [26]. The same study showed the ability of PET to detect distant metastasis as well (Fig. 10). The ability of PET to better stage NSCLC was also demonstrated in a multicenter study that compared FDG-PET to conventional workup (including CT); it resulted in upstaging 27% of patients, thus avoiding unnecessary surgery [27]. PET also plays an important role in staging of patients with lymphoma, leading to a change in stage in 15%-40% of patients [28-29] (Fig. 11). PET also seems to be helpful in patients with ovarian cancer, for evaluation of indeterminate lesions.

**Figure 10**

a. F-18 FDG PET-CT in a patient with lung carcinoma (arrow) with multiple enlarged right hilar and mediastinal lymph nodes (arrow heads) showing intense uptake of radiotracer.

b. Coronal reformatted image showing uptake in left adrenal (arrow) consistent with metastasis.

Images courtesy of Dr. Mohammad Haydar

**Figure 11.** PET-CT in a patient with Hodgkin’s disease.

a. Coronal reformatted CT of body showing enlarged lymph nodes in retroperitoneum (arrow heads).

b. Coronal PET image showing increased uptake of F-18DG in lymph nodes in left supraclavicular, mediastinal, retroperitoneal and left iliac regions.

c. A fused PET/CT image shows the increased uptake in retroperitoneal region corresponding to the enlarged lymph nodes.

Images courtesy of Dr. Mohammad Haydar
and in detecting distant metastasis [30].

In cases of colorectal cancer, CT and endoscopic ultrasound are still the methods most commonly used for initial staging. EUS is the best method for tumor (T-staging) (Fig. 7) as demonstrated in a meta-analysis of data published between 1980 and 1998 that compared the performance of EUS, MRI and CT for T- and N-staging. For T-staging, CT performed poorly with a sensitivity of 78%, specificity of 63% and accuracy of 73% compared to EUS (93%, 78%, 87%). CT also performed poorly for N-staging with a sensitivity of 52% as compared to 71% for EUS [31]. MRI using specific endorectal coils is of great help in tumor staging because of its high soft tissue resolution, but it has limited usefulness in nodal staging. T-stage accuracy was 82% with a sensitivity and specificity of 86% and 77%. For N-staging it was 74%, 76% and 77% [31]. The performance of the new multidetector CT (MDCT) is showing improved results because of its better spatial resolution and speed.

In genitourinary malignancies CT and MRI remain the methods of choice for staging, especially with the current increased use of MDCT (Fig. 12). In the past an overall staging accuracy of 91% has been reported for CT in renal cell carcinoma [32] with most staging errors related to the diagnosis of perinephric tumor spread. MRI is comparable or slightly superior to CT in staging genitourinary malignancies. It has an advantage over CT in evaluating vascular extension, perihilar lymph nodes and tumor extension to adjacent structures [33].

Evaluation of the skeletal system for the presence or absence of metastatic deposits is best done with bone scintigraphy (Fig.13), except in cases of multiple myeloma where the bone scan can be falsely negative. In these cases total body MRI using STIR (fat suppression technique) is very helpful and is superior to skeletal series in detecting myeloma deposits.

The merging of “anatomy” and “function” with the introduction of PET/CT is causing a change in the traditional staging protocols, because this new technology is capable of measuring the biological activity of tumors and allowing accurate localization. Although this will not increase the sensitivity of PET imaging in tumor staging, it does increase the accuracy of PET because of better anatomical localization.

**FOLLOW-UP**

Traditionally, CT has played the major role in the follow-up of solid tumors as well as lymphomas. We relied upon a decrease in the size of a mass to judge its response to chemotherapy or radiotherapy (Fig. 14), or the disappearance of a mass and absence of residual tumor as a sign of successful surgery. The RECIST (Response Evaluation Criteria in Solid Tumors) criteria were introduced to define methodology for uniform evaluation of lesion assessment in response to therapy [34], when evaluating the effectiveness of new drug therapy. These criteria were applied to both CT and MRI. Tumor
response to therapy was judged based on defined changes in tumor size.

Although a decrease in tumor size implies a tumor response to chemotherapy it does not reflect the true biological activity in the tumor. Many times we are faced with situations where there has been a significant decrease in tumor size on cross-sectional imaging, but on follow-up examinations at the end of a chemotherapy course, there is persistent soft tissue density in the tumor bed or at the site of previously enlarged lymph nodes. A question that we are frequently asked by clinicians: “Is this persistent viable tumor?” Our answer based on CT and MR imaging was: “I do not know. If you need more information get a follow-up examination or a biopsy.” A similar problem arises when post surgical or post radiation therapy changes cannot be distinguished from recurrent or residual disease. In these difficult and problematic situations functional and metabolic imaging such as MR spectroscopy or nuclear medicine imaging such as PET and gallium scans can be helpful in differentiating active from burned-out inactive disease.

In the brain and spinal tumors, MRI plays the major role in the follow-up of patients when evaluating the extent of tumor resection and in the follow-up of patients for tumor recurrence after surgical resection. In addition to its anatomical imaging features, functional studies with MRI can help in evaluating patients for tumor recurrence, and in differentiating tumor recurrence from post radiation necrosis. These studies include MR spectroscopy (MRS), perfusion and diffusion imaging [35-37]. In other tumors such as lung, colorectal and breast cancers another form of functional imaging, PET and PET/CT play an important role in the follow-up, restaging and end of treatment evaluation. In addition to its use in the brain to differentiate malignant from benign lesions, MR spectroscopy is finding new applications in prostate and breast carcinoma.

In recurrent colorectal cancer, where curative resection of hepatic metastasis is a treatment option, accurate staging of these patients and ruling out distant metastasis is essential. A meta-analysis by Huebner et al. [38] showed a sensitivity of 97% for PET in detecting recurrent disease and a specificity of 76%. In addition PET led to a change in patient management in 29% of patients, either by up-staging thus preventing unnecessary surgery, or down-staging them leading to curative surgery. In another study by Selzner et al., additional findings on PET/CT, led to a change in treatment strategy in 21% of patients [39]. PET has been shown to be more sensitive than US, CT and MRI in detecting liver metastasis [40] in patients with gastrointestinal malignancies.

![FIGURE 14](https://example.com/figure14.png)

**FIGURE 14**

a. Large lung tumor in right upper lobe (arrow) with enlarged mediastinal lymph nodes (arrow heads).

b. Large liver metastasis (arrow head).

c & d. Post chemotherapy examination shows significant reduction in size of lung mass, lymph nodes and liver metastasis.
Similar results for PET and PET/CT are also seen in patients with lymphoma, where PET not only plays a role in evaluating viable from non-viable residual mass, but also in the detection of extra nodal disease when compared to CT alone [28]. PET and PET/CT can evaluate response to treatment, patients with no FDG uptake after treatment generally have better prognosis than those with residual uptake [41] (Fig. 15).

The use of PET and PET/CT in restaging and evaluation of recurrent breast cancer [42] is emerging as a very important tool in studying these patients, with 30% of patients originally thought to have local disease recurrence were found to have distant metastatic disease. PET plays a similar important role in recurrent lung cancer [43] and thyroid cancer and head and neck malignancies [44-45].

**OTHER APPLICATIONS AND FUTURE DEVELOPMENTS**

With advancement in imaging technology, the delineation of target volumes and the critical structures for treatment planning has become very accurate. This resulted in advancement in radiation therapy technology such as image-guided radiation therapy, 3-D radiation therapy and intensity-modulated radiation treatment [46] (Fig. 16).

With regard to radiation therapy, PET/CT may be particularly useful, because, in addition to the typically excellent staging afforded by PET/CT before treatment, the CT data from a PET/CT examination can also be used for radiation therapy planning, provided the CT data are properly acquired. As reported in the literature [47], PET has a considerable effect on the decision-making process prior to radiation therapy, and treatment changes occur in approximately 25% of patients. These treatment changes include prevention of inappropriate radiation therapy and changes in the intent regarding curative versus palliative radiation therapy, the radiation dose, or the planning target volume [47]. More studies are required to determine the effect of PET/CT in radiation therapy planning. These studies need to answer questions such as: Does the extension of the planning treatment based on PET data improve patient survival or does the reduction of the planning treatment volume result in increased recurrences? [48].

The future of imaging application in oncology is promising. Although FDG-PET has improved our understanding of some malignancies, there are others like brain and prostate tumors that cannot be well evaluated with F-18DG. The development of new radiopharmaceuticals for use in genitourinary and brain malignancies promises
to be an exciting new frontier in PET imaging. New products like Carbon 11 acetate or choline that can be used in prostate cancer (Fig.17), or new labeled amino-acids like F-18 thymidine and ethytyrosine, and some receptor specific markers are emerging for clinical use.

The developments, however, do not stop at this stage. Many believe that the future of medical imaging in general and its oncological applications in particular is in “Molecular Imaging”. Molecular imaging is a new field in imaging that aims to integrate patient-specific and disease-specific molecular information with traditional anatomical imaging technology [49]. PET and PET/CT as well as several nuclear medicine procedures, such as I-123 or I-131 thyroid scans, or antibody imaging are current examples of this technology. However newer agents are being developed to be used in MRI, optical imaging using fluorescent techniques, and ultrasound. Molecular imaging can be used in screening and detection of cancer, staging and imaging of drug therapy assessment.

CONCLUSION

In the last decades there has been several advances and a lot of progress in imaging technology, most of which found its way into newer applications in oncology. In an era where the practice of oncology has become a multidisciplinary approach to the management of the cancer patient, and with the availability of numerous imaging modalities and imaging protocols, the oncologist, surgeon and radiation therapist, should work closely with the radiologist/nuclear medicine specialist to assure the best and most efficient use of the available imaging modalities to adequately answer pertinent questions regarding the patient management.

The future promises us further developments, namely in the field of molecular imaging, which will see further advances in imaging applications in oncology where patient or disease specific questions can be answered.

REFERENCES