PET CT – How much is too much?

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Introduction

The use of ionizing radiation in diagnostic imaging has always required clinical justification. This justification is based on risk benefit assessment for each individual patient at an individual time point within a treatment cycle. Justification for the use of high dose imaging techniques such as Computed Tomography (CT) and Positron Emission Tomography-Computed Tomography (PET CT) examination varies according to the point within the treatment cycle from diagnosis to initial staging to subsequent re-staging or response evaluation. This justification also varies between cancer indications. Various national and international societies have defined some guidelines as to the use of CT and to a greater extent PET CT within the treatment cycle according to cancer type. There has also been significant involvement from insurance companies in the formation of guidelines for imaging particularly with PET CT internationally. Often the decision of when to use PET CT and to lesser extent CT is influenced by the Government policy within the public sector and by insurance company policy within the private sector. In addition to these factors are the clinical responsibilities of the doctors involved in the health care of an individual patient being treated for cancer. In fact, this is the primary decision axis. The responsibility put on the doctor, with the back up of allied health professionals including medical physicists, is to achieve an accurate diagnosis with the minimum of ionizing radiation exposure. Within this framework Monte Carlo risk estimates the risk of a radiation-induced cancer.

How many PET CT should a patient have?

A question that is rarely posed is whether there a limit to the number of C.T. examinations a patient should have in the course of cancer treatment. More specifically for this discussion is there a limit to the number of PET CT examinations a patient should have? After the accumulation of National Oncologic PET Registry (NOPR) data in the USA most national insurance covered patients in the USA are guaranteed access to at least one PET CT during the course of a cancer treatment. Using most international guide lines and insurance company coverage decisions, a significant percentage of patients are eligible for a PET CT during treatment for cancer, which could vary from one study upwards. In clinical discussions there never appears to be an upper limit of the total number of studies performed. The reason for this is obvious, basically that it cannot be defined what particular course an individual patient will have. How long a patient survives with incurable disease will determine how many

investigations an individual patient will have. Essentially this is similar to a situation described in colloquial terms as "how long is a piece of string?" It would seem to illogical to define a maximum number of studies however when looking at the total number of studies and individual cancer patient has over a course of treatment of a period of 3-5 years, often the number of investigations and the total radiation exposure will seem quite high. However when individual cases are looked at, as long as the justification for each test is present, then each test is being performed for a good reason and the risk is appropriate.

The question of how many PET CT studies should a patient have arose after an internal audit in our PET CT unit. The results were surprising in that a significant number of patients had more than 10 PET CT studies performed over a period of 8 years. This finding is both surprising and unsurprising. Patients with metastatic cancer in general are surviving longer. Therefore they are having more tests done. In this setting patients will have C.T. or PET CT. The preference for PET CT will vary from country to country. In our practice I suspect we perform more PET CTs per individual patient however nationally we perform less PET CTs overall, when compared to many other countries in Europe.

Radiation dose is one significant reason for limiting PET CT studies[1]. However cost is also another major factor. The cost differential between PET CT studies and C.T. thorax, abdomen and pelvis studies has reduced substantially in recent years. Some of this is driven by market competition and some is driven by the reduction in the price of ^{18}F fluorodeoxyglucose tracer costs. Insurance companies have also been heavily involved in reducing this cost. Due to the current economic recession pressure for reductions in cost of PET CT studies and to reduce inappropriate use of PET CT has also significantly increased. In some countries the response to increased demand for PET CT has been to outsource imaging. In some European countries the response has been to provide more government-sponsored access to PET CT. The question for a practitioner is how much influence cost should have on deciding on a diagnostic pathway. Nobody can ignore cost, however as patient advocates, doctors cannot allow cost to be only factor that dictates what investigations are used.

In looking at our own internal audit we regarded this as a "washing dirty laundry in public" exercise. The reality is if most practices around Europe looked at the total number of C.T. examinations that they have performed for cancer patients I think they would also be just as surprised as we were with our PET CT numbers. I suspect that many of these hospitals would not admit to such. Locally a set of established national guidelines for PET CT use have been in place for a period of 4 years. Similar to in other jurisdictions, these are guidelines rather than rules. However when a request for PET CT examination is received that is outside of the guidelines this does suggest that a conversation should happen between the referring clinician and the PET CT doctors. Often these indications are discussed at multi disciplinary team meetings. Some national guidelines have been very prescriptive on indications for PET CT but have considerably more vague for indications for CT. Although CT examinations in general have a lesser radiation dose that PET CT studies, they are obviously still associated with substantial radiation dose. Variation in CT guidelines probably reflects a lack of consensus from clinicians as to the exact imaging schedules that patients should have.

[1] For the sake of illustration: "*The dose of an abdominal/pelvic CT is 10 mSv and the dose from FDG administration for the PET component of a PET/CT scan is 5.7–7 mSv. This compares to 7.2 mSv for a barium enema, 0.7 mSv for plain abdominal radiograph, and 0 for nonionizing techniques such as endoscopy*" Halpenny *et al*. Inflammatory Bowel Diseases, Volume 15, Number 6, June 2009 (note from the EAN Editorial Board).

Different approaches and situations

In a relatively small number of centres there is a concept of the "one stop shop" PET CT examination. This is a fully diagnostic PET CT carried out with full dose CT with oral and intravenous contrast as an initial staging study. There is published research for this in certain cancers, for example pancreatic carcinoma. However in our practice we have often used this in the setting of lung cancer, oesophageal cancer, multiple myeloma and in some lymphomas, where a diagnostic surgical excision has been performed. The idea behind this is that a patient who has a very high probability of needing a PET CT study, attends for one study rather than having a CT Thorax Abdomen and Pelvis (C.T. TAP) study performed and then a subsequent PET CT study. This could lead to a lower radiation dose exposure for an individual patient who has a very high probability of needing two studies and also is more convenient for a highly anxious patient. There are arguments against the one stop shop approach including some inaccuracy with SUV measurement, the possibility of using PET CT imaging in a patient who has advanced metastatic disease where treatment will not be altered and the technical complexity of performed post contrast studies leading to higher radiation dose to staff. A "one stop shop" approach probably leads to an increased number of PET CT studies performed overall. A diagnostic related group (DRG approach) to PET CT imaging would necessitate that a "one stop shop" arrangement should not occur. This requires that the decision to perform a second test rely on the first test result. The aim is to reduce overall investigations cost however this prolongs the investigation cycle and as outlined above, in some patients will lead to more radiation exposure.

Reasonable reasons to choose PET CT for staging in general include: where C.T. identifies an abnormality with equivocal interpretation and following analysis at MDT referral is made for PET CT. In addition unexplained clinical symptoms or a substantial rise in a tumour marker where there is no abnormality or change identified on conventional CT, bone scan or MRI investigations to account for this. It may also be reasonable to perform PET CT in a situation where disease was only previously identified on PET CT as opposed to a CT TAP examination. This would not fall within guidelines but often has been more practical in our clinical practice in dealing with individual patients. There is an issue of convenience and anxiety reduction for a small cohort of patients who are under chronic treatment for incurable cancer. These patients essentially have a chronic disease, where attending for PET CT for one test achieves a diagnosis as opposed to attending for up to three alternative tests (C.T. TAP, bone scan and sometimes MRI examination) needed to achieve staging otherwise.

Inappropriate reasons for PET CT staging are the inability to get a C.T. TAP performed on time. This situation arises in the public health service where with cutbacks and at a time of significant increased demand for C.T. examinations, demand cannot be met. This introduces delays which can be from a period of one week to a number of weeks in staging. In current times it is unreasonable to ask patients at a time of major anxiety to wait a significant amount of time to get an answer as to whether treatment is working or not. There unequivocally have been situations in our practice where the inability to access a C.T. TAP on time was matched with ready access through other routes to PET CT which could be obtained in a shorter time frame. PET CT was chosen as the staging test of choice as a result.

Where does patient choice come into this situation? Some patients demand to have a PET CT study performed, knowing that it has higher sensitivity and specificity than CT in staging certain cancers. It is not the practice of health care professionals to respond to all demands from patients, however the ability to deal with demands is influenced by the medico legal environment within a country. If a doctor is to make strong decisions regarding a patient's management, the doctor needs to be supported by the relevant national healthcare service. If this backing is not strong enough the doctor may feel vulnerable and more likely to concede to potentially inappropriate patient requests. This can drive up demand for PET CT imaging. Other situations we have encountered are where a C.T. thorax, abdomen and pelvis study has been performed at an outside institution and where the referring clinician has doubt about the report. Often these doubts can be dealt with at an MDT meeting but sometimes a written finalized report can only be overturned by an alternative investigation. It is too simplistic to think that all C.T. TAP reports can be overturned by an addendum. An addendum may place the Clinician or the original reading Radiologist in a difficult medico legal situation. This nonetheless, again is an inappropriate reason for performing PET CT imaging. For certain cancer indications there are situations where an insurance company or a national provider will pay for a PET CT study, but will not pay for a C.T. thorax, abdomen and pelvis study, for the same indication in the same setting. This can lead to a PET CT study being performed instead of a CT-TAP. This situation reflects anomalies in the insurance market, which usually are resolved over time, once the problem is identified.

Despite the construction of imaging guidelines for PET CT there still is some room for interpretation. The guidelines tend to be moderately complex and there are a number of people interpreting these guidelines including the referring oncologist, the radiologist or nuclear medicine physician and insurance company administrators. This can lead to different opinions or different reasons for performing the PET study. Within our national guidelines there is a paragraph outlining some flexibility for imaging in individual cases:

> "*There are clinical indications for PET CT that do not meet specific guidelines outlined above, but where expert medical opinion indicates that the imaging procedure would have a major impact on patient management. These indications are typically discussed at a local multi disciplinary team meeting (MDT). It is anticipated that PET CT referrals for these indications would be reviewed by regional approval board, or officer or by an expert in PET CT at the PET CT centre prior to a decision to proceed with imaging. In general the process of guidelines or rules covering PET CT imaging is leading to a broader range of indications for PET CT over time rather than a smaller range*".

In our own practice, in general we perform more full dosed CT as part of PET CT than other centres in Europe. This reflects a greater use of the C.T. component of PET CT for diagnosis. Our PET CT readers are dual Fellowship level trained readers in Radiology and Nuclear Medicine. The broad consensus within our imaging group is that the C.T. component contributes significantly to the interpretation of PET CT. The use of full dose or a local protocol of medium dose C.T. as part of PET CT studies is not necessarily limited to initial diagnosis studies. There are some patients where restaging examinations are performed with full dose. Some studies have individual protocols for example a specific protocol for multiple myeloma patients involves whole body imaging with low dosed C.T.

Other factors of concern in the decision

Upon review of the total number of PET CT examinations per patient over an 8 years period, including 14,000 patients, we identified a relatively small number of patients who have had more than 10 PET CT studies performed. On analysis of these patients the largest single group came from metastatic breast carcinoma with the next highest indication being colorectal carcinoma and the third most prominent indication was lymphoma. Other patient indications included multiple myeloma, gastro intestinal stromal tumour, melanoma, vulval carcinoma and renal cell carcinoma. On analysis of these patients 89% of cases had substantial life threatening disease where the radiation dose associated with either a C.T. TAP or PET CT study was unequivocally justified. In the remaining 11% of cases we could establish justification in most of the studies performed, but not in all cases. Following this we have decided to change our approach to protocoling patients for PET CT with more rigorous protocoling for any patient who receives more than 8 PET CT studies or referral for any more than 3 PET CT studies in a 12 month period.

If PET CT is being used for multiple studies, then very close attention must be paid to the C.T. component of the study, which contributes most of the patient dose. All modern C.T. reconstruction techniques need to be used. In addition access to the most modern PET CT imaging scanner technology helps with dose reduction. Along with manufacturers we have looked at C.T. dosage and have achieved substantial reductions in this.

Another factor that specifically causes concern, is the risk of cataract formation. With most protocols PET CT imaging is commenced at the base of skull. For certain tumours, imaging should start at the skull vertex, including head and neck cancers, melanoma and according to some protocols, for lung carcinoma. This is a problem that should be addressed by careful radiography technique and the use of low dose C.T. as much as possible. Radiation induced cataract formation is a deterministic effect, as opposed to the risks of cancer induction, which more typically preoccupies prescribers.

The cohort of patients who are suffering from chronic metastatic disease, in some cases, have assumed a risk profile that is now similar to some other serious chronic diseases, rather than the conventional perception of cancer survival. In our practice breast cancer staging is probably the most controversial indication for PET CT. A classic scenario is a patient with incurable metastatic bone disease, on hormone therapy, where there is a suspicion of progression of bone disease or development of early soft tissue disease. The development of soft tissue disease is associated with a more rapid progression of disease. The question that must be asked in each individual situation is how important is the answer that the study will give and as to what impact this is going to have on patient treatment. Often the impact of the study is a change in treatment from hormone treatment to the use of chemotherapy. This is a major treatment decision. The treatment decision has an impact on the patient in terms of side effects. Chemotherapy treatment is also potentially dangerous with both associated morbidity and mortality. The treatment is also expensive, considerably more expensive than PET CT. In our experience the level of confidence regarding the progression of disease, particularly in patients with bone metastases with breast carcinoma, is almost always higher with PET CT imaging. International guidance regarding when to use PET CT in this situation, for patients with incurable disease, is very weak. It may be deliberately weak. Often a local decision must be made.

When a local decision is made it is difficult to decide whether this decision is the right or wrong decision. Essentially when does this type of practice make you an "outlier"? The easy solution is to say "don't use PET CT in this situation", a more balanced answer would be to prove that the use of PET CT prolongs survival, or lowers treatment costs. There is very little data available on the influence of PET CT usage on survival for patients in this situation. However the cohort of patients undergoing treatment for chronic incurable metastatic disease, who require intermittent staging, is constantly increasing in size and this is an issue that should be addressed.

There are no guidelines world wide for the total number of C.T. TAPS or PET CT studies a patient with metastatic cancer should have in a lifetime. It is impractical to have such a guideline. The response to this situation is to justify each individual test at a particular point in time for an individual patient. Focus should be on particularly reducing the C.T. dose associated with C.T. TAP examinations and the C.T. component of PET CT. In this setting therefore is it reasonable to perform PET CT more than 10 times in some patient groups? I would challenge doctors in charge of imaging in Europe to look at the total number of C.T. TAPS performed on their patients with chronic metastatic disease. I think the results would be surprising to most. In looking at this you should also look at bone scans performed. Consideration should be given to time and anxiety associated with performing MRI in patients where C.T. TAP is non diagnostic.

In summary

PET CT is an extremely useful examination in the correct clinical setting. It is a high radiation dose examination where use must be carefully justified and optimized. Justification is complex in patients with life threatening metastatic disease who survive over a number of years. The longer survival of patients is a welcome and positive development; we shouldn't be surprised that we are going to use more ionizing radiation in this patient group.