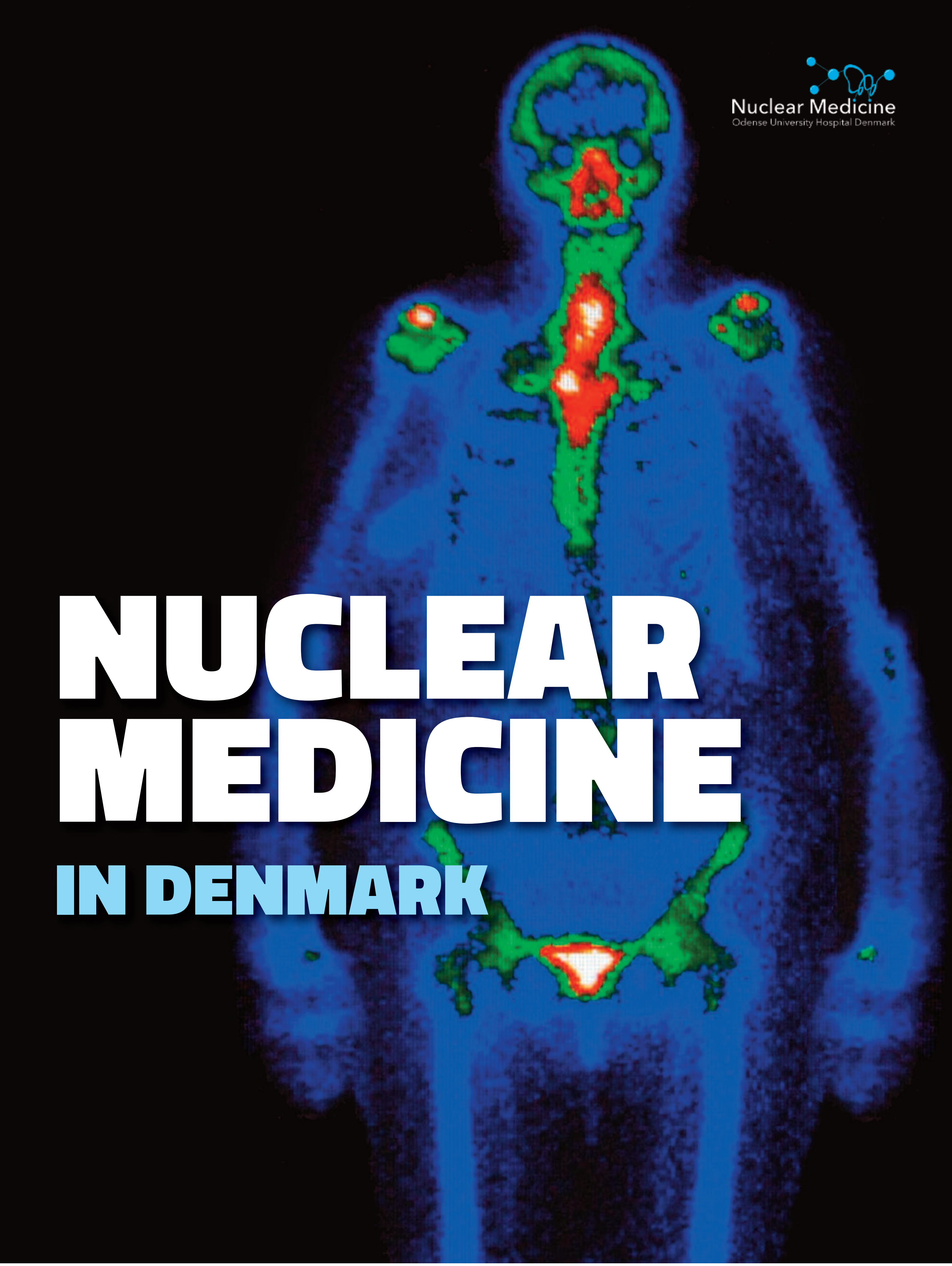

Nuclear Medicine
Odense University Hospital Denmark

NUCLEAR MEDICINE

IN DENMARK

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Healthcare goes nuclear

Adjacent Digital Politics gives thought to nuclear medicine in modern day healthcare and the role the World Federation of Nuclear Medicine and Biology (WFNMB) plays in promoting this specialism...

In the 21st Century there are a number of healthcare challenges that can have a debilitating and life changing impact on people's lives. Throughout the world there are people living with, and researching diseases such as cancer, and new technology has had a major impact on how we treat and diagnose such diseases to help people live independently and comfortably.

The World Health Organisation (WHO) reported that 14m people developed cancer worldwide in 2012, and the global death toll from cancer rose to 8.2m in 2012 (1). In modern healthcare, nuclear medicine plays a vital role in advancements when tackling life-threatening diseases, such as cancer.

There are over 2500 nuclear medicine units in Europe, with over 5000 medical imaging cameras between them; however, the number of centres combined is limited due to constraints of pharmaceuticals and nuclear protection regulations.

Extensive research is necessary in order for nuclear medicine to develop and continue its work in tackling major healthcare challenges. In addition, partnerships between academic researchers and industry have an integral role to play in this development.

Although one usually associates the word 'nuclear' with bombs and radioactive material, these radioactive materials are essential in modern healthcare to facilitate some common medical procedures which might otherwise be unavailable, such as x-rays, scans, radiation therapy, and CT scans.

Remarkable advances in technology have had a prominent role in propelling the growth of nuclear medicine practice over the last few decades. Due to evolving technology, there have been many changes since the first gamma camera was introduced in the 1950s.

Current procedures can be pivotal in recognising and diagnosing some of the most challenging diseases that plague 21st Century medicine. For example, radiation therapy is one of the key treatments for cancer patients, and without such a treatment it could be hard to see the exact location of a patient's tumour and its progression.

The technique used is nuclear imaging (PET scan), which creates computerised images of the human body in order to locate chemical changes that take place in the tissue.

The World Federation of Nuclear Medicine and Biology (WFNMB) support the education efforts for nuclear physicians, physicists, technologists and other nuclear medicine scientists, especially from the developing world. The main aim of the WFNMB is the progress and promotion of nuclear medicine and biology throughout the many regions of the world.

The Federation was founded in 1970 at the third ALASBIMN congress in Mexico City, with the First World Congress of Nuclear Medicine held in 1974 in Japan. One of the key features of the WFNMB is the integration of developed and developing countries. They have become a major international forum for the presentation of all aspects of basic, applied and clinical nuclear medicine.

By running extensive education programmes, the Federation works with member societies to offer educational programmes and information to help individual nuclear physicians stay current and provide the best possible nuclear medicine practice to the public. (2)

Organisations like the WFNMB play a vital role in ensuring nuclear medicine is at the forefront of research and development, not only in Europe but worldwide. It is important that clear and effective communication exists between researchers and healthcare professionals. At a European level, the European Association of Nuclear Medicine (EANM) has ensured effective cooperation and coordination – a necessity for nuclear medicine.

Both the WFNMB and the EANM have given nuclear medicine the platform it needs to promote the development of nuclear medicine at a global level. The World Federation for Nuclear Medicine & Biology in particular works towards developing cooperation between groups, societies and associations formed on a national level.

As well as representing with one voice all nuclear medicine activities to the World Health Organisation (WHO), the International Atomic Energy Agency and other appropriate organisations, they also facilitate the exchange of scientists between the member groups and association to help share knowledge.

Nuclear medicine in healthcare has certainly come a long way since the 1950's, and continual research and development will ensure further progress in the years to come. Modern day healthcare has benefitted from new treatments being developed through nuclear medicine, however there is still more to be done.

Through organisations such as the WFNMB and EANM, nuclear medicine can only be further understood and developed. As long as the funding and enthusiasm is available, this specialised area of healthcare can continue to deliver outstanding achievements for improved global health.

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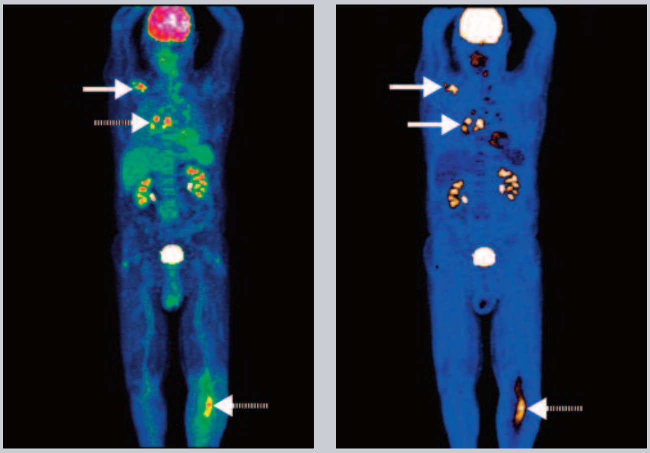

Figure 1: All-in-one PET/CT. 68 year old male with a history of lung cancer and deep venous thrombosis – now admitted with fever and bacteraemia of unknown origin. PET/CT demonstrated (1) the already known lung cancer (dotted arrow), (2) the also known deep venous thrombosis (interrupted arrow), and (3) a focus in his right upper arm, chest, and neck (solid arrow) consistent with a muscular abscess.

Nuclear medicine in the 21st Century

On the move to individualised precision diagnosis and therapy

Health expenditure has reached above 10% of the gross domestic product in most Western countries with an upward trend indicating that 20% may already be reached in the present decade, unless something drastic can turn the tide (1). Prevention is the vision, but many such efforts remain to translate into disease regression and major economic savings. Therefore, it may be worthwhile to examine if current principles for disease management can be changed in a cost-effective way.

Nuclear medicine offers a unique instrument that may, in several diseases, accomplish this task if used early and strategically in the course of disease. The mantra is: individualised diagnosis and therapy. What is needed is an 'instrument' that can change the mindset of doctors and healthcare decision-makers from conventional to more unconventional thinking and doing. This instrument in the hands of nuclear medicine is molecular imaging.

A correct diagnosis is a must for rational therapy. Diagnosis alone is not enough because even a well-known disease is a continuum in activity, extent, and severity; factors all of which are modelled by the organism that harbours it. In contrast, what is presently considered the highest level of medical evidence are results retrieved from so-called randomised clinical trials based upon the premise that groups of patients with the same disease traits comprise largely of comparable individuals. This premise is seldom true, but necessary, because otherwise we cannot apply statistical methods to determine with what degree of probability we can assume that a drug given to group A is better than another given to group B.

This dilemma defines a needed shift in modern healthcare from "evidence-based (cohort) medicine" to "knowledge-based (personalised) medicine" as proposed by Dr. Patrick Hunziker in Basel, Switzerland. As head of an intensive care clinic, he has to make decisive decisions for each of his critically ill patients because they do seldom belong to an easily recognisable and clinically well-defined group. According to him we need refined and computational science tools for personalised medicine in clinical practice to achieve more effective, safer and affordable therapies with "a perspective of cure instead of disease suppression" (2). Molecular imaging is one of the ways to go to achieve this goal.

Principle

Using almost infinitely small amounts of substance and radioisotopes to label it, the radioactivity representing a

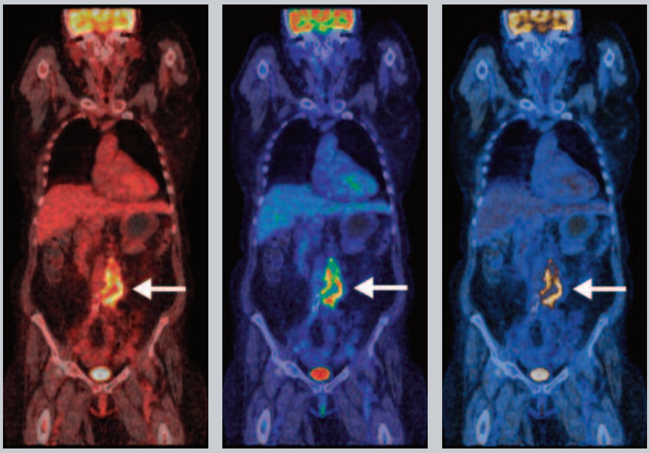

Figure 2: Vascular prosthesis infection. 66 year old female with an aortic vascular prosthesis. Vascular surgeons suspected prosthesis infection, CT was equivocal. PET/CT showed focal tracer uptake (arrow head) consistent with active infection – confirmed by succeeding surgery.

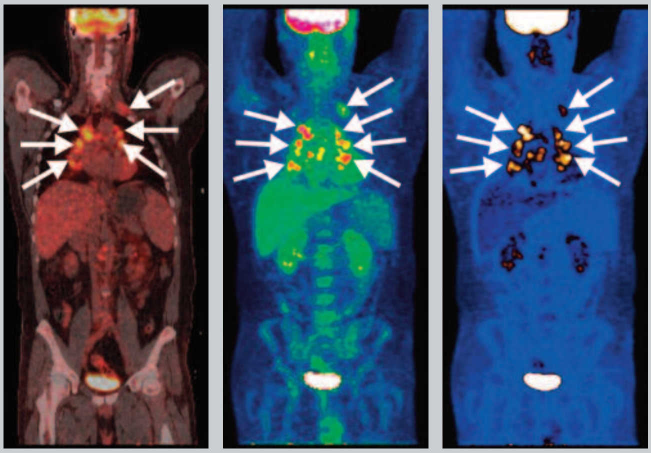

Figure 3: Active sarcoidosis. 38 year old male with fever of unknown origin and previous treatment for sarcoidosis which was considered inactive and not responsible for fever. PET/CT on the other hand demonstrated marked tracer accumulations indicating ongoing inflammation in mediastinal, hilar, and periclavicular lymph nodes (arrows) consistent with active sarcoidosis.

certain molecule and its handling in the organism, can after ingestion or injection be detected, measured and monitored from outside the body by a PET[1] scanner with a sensitivity and precision unsurpassed by other known methodologies. In this way, disease processes can be detected, and their extent and activity be graded and used as guidance for therapy in the early phases of disease (when cure is still an option). All biological molecules can in principle be made radioactive, traceable and measurable from outside the body. This is no longer just a vision, but a realistic possibility due to recent decades' advances in biomedicine and medical technology. Being 10^3-10^6 times more sensitive than conventional imaging, PET imaging is a core element of future personalised medicine. Radiation to the patients is not an issue, since the amount of radioactivity used for imaging is far too low to cause any damage, a fact that is now recognised by the American Association of Physicists in Medicine. This strongly discourages predictions of hypothetical risks associated with such low radiation doses, because they may "cause some patients and parents to refuse medical imaging procedures, placing them at substantial risk by not receiving the clinical benefits of the prescribed procedures" (3).

Diagnosis

With PET/CT[2] imaging the entire body can be examined in one single examination without any inconvenience to the patient and quite often yielding unexpected findings (Figure 1). What else makes this method unique? Imagine a city with streets and traffic seen from above as on a map. Conventional imaging provides a frozen picture allowing determination of the number and position of cars, bicycles, pedestrians, and various traffic lights. However, it does not tell anything about the dynamic processes going on in the photo. It cannot discern who is alive and who is dead, what is moveable and what is not. A pattern is revealed, but it's deeper meaning remains uncertain. With dynamic molecular imaging everything becomes immediately clear: houses stand still, people and vehicles move, red light means stop, green means go, and so on. All of a sudden, the static information turns into a dynamic system, the rationale of which will soon become apparent and yield information of ways to regulate, modify and improve, if needed. This is the beauty of molecular imaging. With careful examination, one may even understand cause and effect.

Many diseases are not detectable by conventional imaging, particularly not in their early phases when they are more amenable to therapy. This is the case with various forms of infectious and non-infectious inflammation (Figure 2) including rarer types like sarcoidosis (Figure 3). Inflammatory diseases which are usually diagnosed from their typical location, like in the skin, the kidneys or the intestines may turn out to be more universal, localised also in vessels or other inner organs explaining hitherto unexpected or equivocal manifestations. Cancer may go undetected even if suspected because of poor general condition, weight loss or previous cancer therapy (Figure 4). PET will often disclose both a primary tumor and its metastases when other methods have failed (Figure 5). Moreover, PET is able to categorise cancers in non-aggressive, mildly aggressive and severely aggressive types. Promising new applications are early detection and quantification

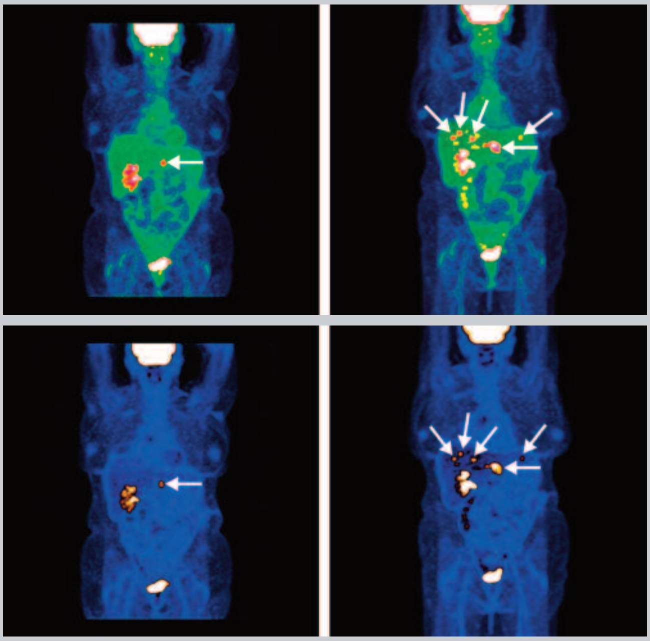

Figure 4: Recurrent gastric cancer. 55 year old female previously operated for resectable gastric cancer. Post-surgery follow-up PET/CT (left) showed a focal hotspot consistent with residual/recurrent lymph node metastasis. CT and endoscopic ultrasound were normal, so the surgeons considered the PET/CT result false positive. PET/CT 3 months later (right) revealed progression of the primary lesion and new liver metastases.

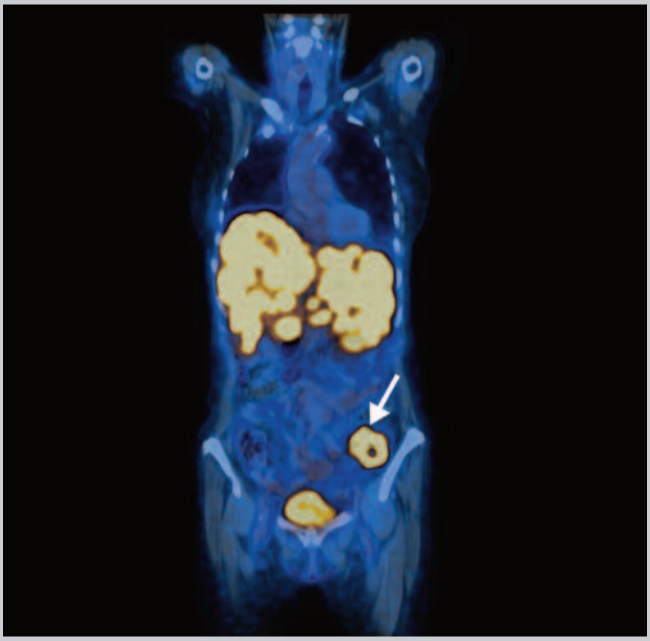

Figure 5: Cancer of unknown primary. 57 year old female with multiple liver metastases incidentally detected by a CT scan following a traffic accident, but where was the primary tumour? Succeeding PET/CT confirmed the liver metastases and revealed the primary tumour situated in sigmoid colon (arrow head).

of cardiovascular arteriosclerosis, years or decades before otherwise detectable, and, similarly earlier diagnosis of the early stages of osteoporosis – much quicker than with conventional methods.

Therapy

Symptoms, clinical findings, biomarkers in blood samples and conventional imaging may not be sufficient to characterise precisely the disease of the individual patient and predict outcome with or without therapy, treatment efficiency, and the risk of side-effects. With its high sensitivity, PET imaging is ideally suited for these purposes including in-advance testing of treatment responsiveness and monitoring of response to therapy in the shape of disease progression or regression (Figure 6). This has become increasingly pertinent when it comes to advanced and expensive bioengineered cancer chemotherapy, where guidelines dictate its continued use for weeks/months, as long as CT scans show sizable tumour formation. Because in many such cases, molecular imaging may have shown that active tumour cells have gone a long time ago (Figure 7). This particular application is under heavy scientific study, because early discontinuation of cancer therapy, or swapping to an alternative, and potentially more effective or endurable treatment, may spare the patient some inconvenience and unpleasant side-effects, and save the community a lot of money.

Perspectives

In short, while structural imaging displays differences in tissue density, water content, etc., molecular imaging provides understanding and quantification of molecular processes in the body. It utilises molecular targeting in the shape of disease-specific metabolites, antibodies, peptides, nanoparticles and nucleic acid-based engineered biomolecules, i.e., techniques which in the future will have a major impact on early and improved diagnosis, monitoring of treatment response, pre-clinical and clinical drug development, and above all, personalisation of medicine. A promising new option is to use the same or similar molecules that can target and image cancer as vehicles for special radioactive isotopes that will find and irradiate cancer cells inside the body to make them unable to proliferate and give rise to new metastases. Depending on the type of radioisotope, another advantage of this approach appears to be considerably fewer severe side-effects than with external radiation therapy or chemotherapy.

Despite these many advantages, the concept of molecular imaging has not yet penetrated deep into the minds of the medical community and medical decision makers, which sometimes appear to be somewhat stuck in traditional 20th Century thinking. Hospitals adopting molecular imaging will rapidly move to the forefront of advanced patient management at lower cost, fewer adverse side effects, and higher success rates.

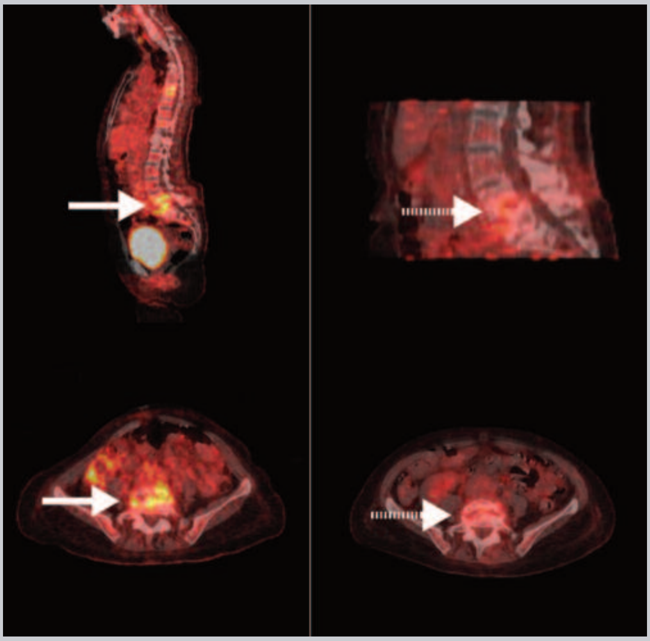

Figure 6: Therapy response evaluation. 79 year old female with thoracic and lumbar vertebral disc infection (spondylodiscitis). Before treatment, PET/CT (left) showed marked tracer uptake at both locations (solid arrows). PET/CT after 4 weeks of treatment demonstrated almost normalisation, while CT remained virtually unchanged (interrupted arrows).

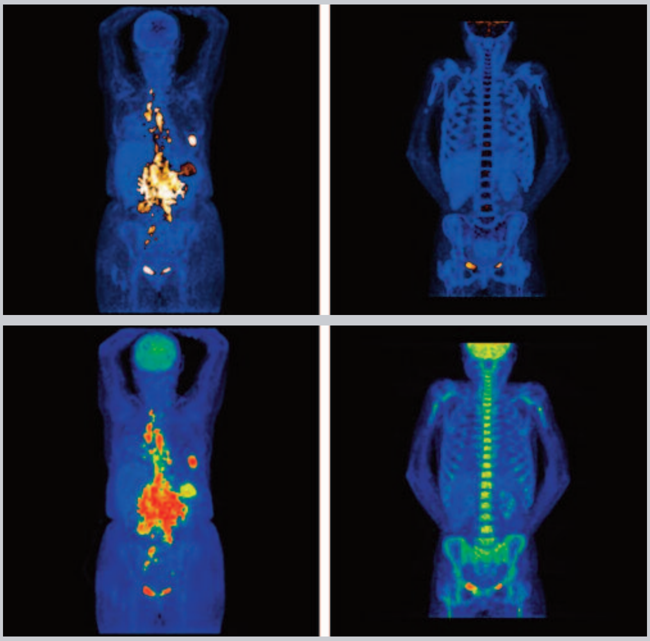

Figure 7: Lymphoma. 60 year old female with non-Hodgkin's lymphoma. PET/CT before treatment (left) showed marked tracer uptake in multiple lymph nodes throughout the body consistent with dispersed lymphoma. PET/CT after 3 cycles of chemotherapy (right) demonstrated complete response to therapy with no tumour masses left, but increased bone marrow uptake indicating suppression caused by chemotherapy.

Odense Spring Meeting

PET imaging in the Nordic European countries started in Sweden in Uppsala and Stockholm in the late 1970s, followed by Turku in Finland (1988) and Copenhagen (1988) and Aarhus (1993) in Denmark. The Department of Nuclear Medicine in Odense dates back to 1957, but did not get its first PET/CT scanner until 2006. Now, Denmark is one of the countries in the world with the highest density of PET/CT and PET/MRI[3] scanners per capita, namely about 30 scanners in total or about 1 scanner per 180,000 inhabitants. Odense was not part of the "PET Society" until 2006. Now it has one of Denmark's largest PET centres with cyclotron, radiochemistry, four PET/CT scanners, small animal PET/SPECT/CT, a 5th clinical PET/CT, and a new generation PET/MRI scanner on the 2014 horizon. This is celebrated by the organisation of the first "Odense Spring Meeting" on 12-14 May 2014, subtitled: "Molecular Imaging: Solution to Tomorrow's Health Care?" – For details, see www.odensespringmeeting.com.

[1] PET = Positron Emission Tomography

[2] PET/CT = PET/Computerised tomography: name of a scanner type combining molecular (PET) and structural (CT) imaging

[3] PET/MRI = PET/Magnetic Resonance Imaging – another type of combined molecular/structural scanner

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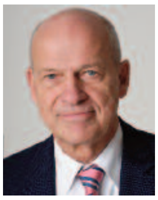

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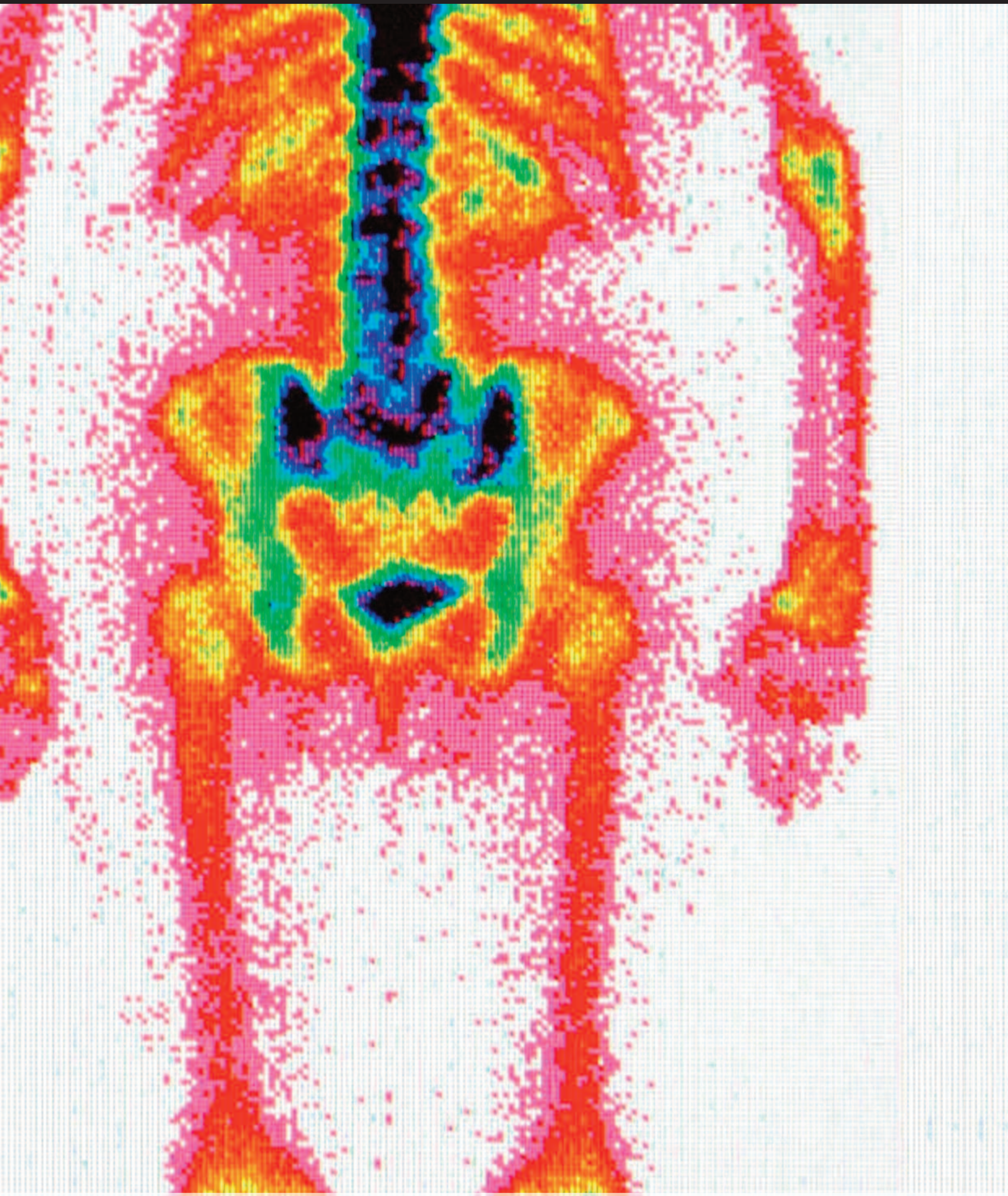

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