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Campaign to safeguard the future of MRI

MEPs Dr Peter Liese and Mr Stephen Hughes have joined healthcare professionals and European patient groups in a campaign to safeguard the future use of Magnetic Resonance Imaging (MRI).

In early 2010, the European Parliament and Council is due to be sent a proposal from the European Commission to amend the physical agents directive (2004/40/EC) on electromagnetic fields. The revision has come about as a result of the concerns raised by the campaign group, Alliance for MRI, and recognition by EU institutions that the Directive may curtail the use of MRI to the detriment of patients in Europe.

The European Society of Radiology (ESR) and the European Federation of Neurological Associations (EFNA), both members of the Alliance, are calling on members of the newly elected European Parliament to exclude all uses of MRI from the exposure limits set in the Directive.

The exposure limits 'have now been proven to be detrimental to patient care, most notably restricting and limiting the use of MRI in interventional applications and in imaging vulnerable patients and children where closer patient contact is required.

'PATIENT ACCESS TO MRI IS THREATENED DUE TO A HYPOTHETICAL RISK TO WORKERS'

'Furthermore, new research and developments in MRI will be severely restricted as will routine cleaning and maintenance of MRI equipment,' a statement from the Alliance said.

Dr. Liese MEP said, 'I hope the position of the Alliance for MRI will be supported by members from all sides of the house.'

Stephen Hughes MEP, a long-standing supporter of the Alliance said. 'Comprehensive safety guidelines already exist for the use of MRI and indeed the UK and many other member states have an established safety framework for both patients and staff.'

Professor Gabriel Krestin, Chair of the Department of Radiology at Erasmus University, Rotterdam, said, 'MRI is one of the most significant developments in medical technology and in Europe we are at the cutting edge of developments in this field.

'Worker protection is taken very seriously, however the current legislation threatens patient access to the benefits of MRI due to a hypothetical risk to workers. The Alliance for MRI hopes that its position will be reflected in the forthcoming proposal from the European Commission and we look forward to support from the European Parliament and the Council. As MRI is used in a controlled environment, comprehensive guidelines can guarantee the safety of workers without the need for EMF exposure limit values.'

Imaging biomarkers and RECIST

Barriers to be overcome before functional and molecular imaging can be incorporated into the Response Evaluation Criteria In Solid Tumours (RECIST) were discussed at a scientific symposium at the Congress (Berlin 20–24 September, 2009).

Dr Elizabeth Eisenhauer (National Cancer Institute of Canada, Kingston, Ontario) presented highlights from the revised RECIST guideline, version 1.1 (published as *EJC Special Issue 45:2 2009*). Changes include a reduction in the number of lesions to be assessed, from 10 maximum to 5; and from 5 to 2 per organ, maximum. Assessment of pathological lymph nodes has been incorporated; confirmation of response is now required only for trials where this is the primary endpoint; and disease progression has been clarified. New imaging guidance is incorporated.

A key question considered by the working group in developing RECIST 1.1 was whether it was time to move from anatomic unidimensional assessment of tumour burden to either volumetric anatomical assessment or to functional/molecular imaging with PET or MRI.

'The Working Group did not believe there was sufficient standardisation and wide-spread availability to integrate these alternative assessment methods into all aspects of RECIST,' Dr Eisenhauer said. 'A key aspect of further RECIST working group activity

(continued on page 3)

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ECCO 15–34th ESMO Multidisciplinary Congress

Young voices 'are not being heard'

Teenagers and young adults with cancer may experience prolonged suffering, acute distress and intense frustration over symptoms which are not taken seriously, according to Ms Susie Pearce (University College Hospital, London).

Speaking at a 'Experiences of Care' session at the Congress (Berlin, 20–24 September, 2009), she said: 'While being diagnosed with a potentially life-threatening disease is a distressing experience for any patient, a cancer diagnosis, and the process leading up to it, can have a particularly poignant impact on teenagers because that stage of development already presents significant challenges in developing independence, identity and in coping with the world. Research in this area has been limited and better understanding of the complexities of their experience in the pre-diagnostic period is crucial if we are to provide the most comprehensive and sensitive care and improve their outcomes.'

There is a small evidence base on teenagers and young adults with cancer, Ms Pearce said. Those aged between 15 and 24 years account for less than 2% of all cancer cases worldwide. However, these rates are twice as high as in children and long-term outcomes and survival rates have improved less than for other groups. Delayed diagnosis is a major issue.

In the study (funded by the UK charity, CLIC Sargent), researchers talked directly to 24 young people, aged between 16 and 24 years, about their experience from the time of first symptoms to diagnosis. Interviews took place 2–4 months after diagnosis and participants' medical notes were analysed.

The study, conducted in collaboration with Professor Faith Gibson (Great Ormond Street Hospital, London) and Dr Daniel Kelly (Middlesex University, London), revealed a pattern of young voices not being heard, delays in diagnosis and a misconception that young people don't get cancer.

'While symptoms in some young people were promptly recognised by GPs and referred to specialists quickly, other patients recounted tales of protracted periods of suffering, with rationalisation of their own symptoms or numerous disappointing visits to doctors and hospitals before the cancer was diagnosed,' said Ms Pearce.

'One consistent thread through these stories is young people's perception that they were not being listened to and that cancer was being ruled out on age alone.'

In one case, a 22-year-old woman who was diagnosed with colon cancer that had spread to the liver recounted a frustrating battle to be taken seriously after 9 or 10 years of suspicious symptoms such as food aversion, abdominal pain, frequent diarrhoea and rectal bleeding and two separate diagnoses of familial adenomatous polyposis, or FAP, a hereditary syndrome that carries a high risk of colon cancer. After her participation in the study, this young woman died.

'GPs TYPICALLY SEE ONE CASE EVERY 15 YEARS'

The time period between first symptoms and diagnosis ranged from 8 weeks to 11 years. The study reported the sense of relief felt by patients when they finally entered specialist care and felt that they were in safe hands with experts in whom they had confidence.

'The stories related here are, sadly, far from unique. Doctors should be making urgent referrals when children or young people come to see them several times with the same problem and persistent parental anxiety should be sufficient reason for referral,' said Ms Pearce.

Looking ahead, the study group recommend interventions such as better education in schools and universities, and of health professionals, including school nurses, university health centres, GPs and Accident and Emergency staff, so that classic signs are investigated promptly.

Ms Pearce said that the issue of delayed diagnosis is complex: 'In the UK, for example, GPs typically only see one teenage and young adult cancer patient every 15 years. It's difficult for them. Also, from the patients' perspective, it's probably very difficult at this age to articulate effectively one's symptoms to a healthcare professional.'

Participation in clinical trials is another area where teenagers and young adults do poorly, Ms Pearce said. Other issues that need attention include specialist care, improved understanding of the role of families and friends of patients, and the views of healthcare professionals.

'Essentially, we need to know more about the whole cancer trajectory for teenagers and young adults,' said Ms Pearce.

Danish research presented at the same session highlighted the potential role of oncology nurses. A network-based nursing programme was implemented at a Danish oncology youth unit, with the aim of extending nurses' reach into the young people's wider social network.

The study was comprised of in-depth interviews and observation of the young people, aged 15–22. The researchers showed that oncology nurses can, through interaction with the patients and their significant others, promote the social support of teenagers and young adults with cancer by preserving, establishing and strengthening family relationships and social networks during the treatment period.

Study investigator Pia Olsen (Aarhus University Hospital, Denmark) said: 'Meeting the needs of teenagers and young adults with cancer is a complex and highly demanding practice that needs to be addressed by nurses, educators, researchers and health policy makers.'

Ms Pearce agrees: 'Practice, research and education need to be linked and subsequently fed into policy in order to achieve the necessary improvements in teenage and young adult cancer care.'

(EJC Supplements 2009 7. 2: 234 #4170; EJC Supplements 2009 7. 2: 235 #4172)

Robert Day-Webb

ECCO 15–34th ESMO Multidisciplinary Congress

Imaging biomarkers and RECIST (*continued from page 1*)

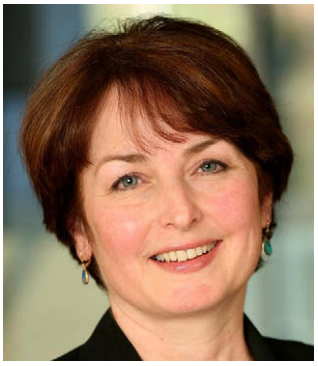
will be to stimulate international standardisation and assessment of these modalities in rigorous clinical validation studies in the next years, to determine where and how they add value to standard anatomical imaging.

'The next generation of guideline, we hope, will have clarity regarding in which circumstances and tumour type these new imaging techniques can supplement or replace anatomical monitoring.'

At the same session, Dr Bruno Morgan (University of Leicester, UK) said that aspects of the CT measurements currently used in RECIST will need to be mimicked in any novel imaging criteria. The CT measurements are standardised, practical and tolerable – virtually all centres can do it and virtually all patients can undergo it – and reproducibility 'isn't bad'.

'CT-defined progression is a pretty good endpoint. At 6 months out, if CT says the tumours are getting bigger, the patient is getting worse. There are very few exceptions to that.

'The problem effectively is that CT measurement is slow and it's not



Dr Elizabeth Eisenhauer

necessarily linked to the biological activity of the drug,' he said.

Imaging shows that the effect is happening in the tumour, and whether it is happening in all tumours. But Dr Morgan said, 'Almost without exception, the imaging biomarkers we are trying to use are more expensive, more difficult, less reproducible and less available.'

With dynamic contrast enhanced magnetic resonance imaging (DCE MRI), information about organs is gleaned from different patterns of enhancement. But the scanner adjusts various parameters to get the information, so that a brain scan is different from a liver scan, for example. 'It's about slice thickness and resolution, contrast injection times, how we define regions of interest around tumours. At the moment, it's slightly arbitrary and is the decision of the radiologist or the oncologist who is doing the analysis,' Dr Morgan said.

Interpretation of data is difficult. A phase I study in Leicester found that an anti-angiogenesis agent called PTKZK gave dramatic results on enhancement. There was a strong dose response curve and even a clinical response correlation: 70% people who had a good MRI response (defined by greater than 40% reduction in enhancement) had stable disease or better. Only 20% of those who failed to get a good MRI response would stabilise.

'But the phase III trials on this agent failed. They failed to show an advantage of adding this agent to FOLFOX or FOLFIRI. We have to ask ourselves the question Why? It looked so good,' Dr Morgan said to the meeting.

'We have to ask – is the DCE MRI a surrogate clinical endpoint? Is it relevant to the intended benefit to the tumour? We have to believe that it is, particularly when we see that the people who got the response did better than those who didn't,' he said.

One possibility is that the imaging biomarker predicts the action of a single agent, and not its effect in combination. It might be that those who respond have a particular histological subtype, and the response is a predictive marker. Or that it's a prognostic marker, identifying those who would live longer anyway.

Issues relating to the use of PET are different, Dr Morgan said. The slides are easy to understand, and work well in a multidisciplinary conference. But although the response is 'probably a good surrogate clinical endpoint', it is not specific for drug efficacy, he said, and it may be that viable cell count is being measured. Further, not all tumours take up FDG, especially in second or third line therapy. Inflammatory response may hide response in early treatment. PET is expensive and delivers high radiation doses, not normally a concern in advanced cancer but more so in lymphomas in people who are expected to be cured. Finally, it is not yet widely available.

In planning an imaging biomarker study, issues of affordability and practicality need to be taken into account, Dr Morgan said. 'The joy of dynamic CT for volumetric measurements is: we were doing CT anyway. We may be doing MR anyway, but it's not so easy to say that for PET.'

In phase III studies, protocols need to be rigid so that techniques are clearly understood and reproducible. But phase I and II trials are completely different, he said. Rigid protocols in these earlier trials 'actually may limit development' because they would prevent radiologists from adapting the technique to that particular tumour or organ type. 'If we're going to use [novel imaging] in phase I and phase II we need to have an open mind,' he said.

'IMAGING BIOMARKERS ARE MORE EXPENSIVE, MORE DIFFICULT, LESS REPRODUCIBLE AND LESS AVAILABLE'

He said that in early trials, researchers do not have to satisfy regulatory bodies because the decision is mainly about whether a phase III registration study is set up. Even in phase III 'it may be that we don't need a lot of novel imaging to decide whether [the agent] helps patients or not.' PET as a progression marker could be helpful and Dr Morgan said the RECIST Working Group is addressing the issue of how to incorporate progression on PET – which not all patients will have been offered – without statistically affecting the study.

(EJC Supplements 2009 7:2 5 #11; EJC Supplements 2009 7:2 6 #12)

Helen Saul

16th International Meeting, European Society of Gynaecological Oncology (ESGO) Belgrade, Serbia; 11–14 October 2009.

HPV jabs for boys?

A global vaccination programme against human papilloma virus (HPV), which includes boys as well as girls, could lead to the virtual disappearance of cervical cancer, predicted Professor Harald zur Hausen (German Cancer Research Centre, Heidelberg, Germany).

In a keynote lecture, Professor zur Hausen said that HPV prevention has important implications for men's health: 'If we wish to achieve eradication within a reasonable period of time, we will need to vaccinate both sexes.'

Some cancers associated with HPV infection, such as anal and oral cancer, are more common in men, and genital warts occur in both sexes. 'There is good reason to vaccinate boys before the onset of sexual activity,' he said.

Future reductions in production costs and development of cheaper vaccines will make wider vaccination a realistic option, he said, and a major reduction in HPV 16 and 18 would probably enable the interval between currently used cervical screening tests to be extended. The introduction of self sampling by women, using new tests for HPV DNA, could also help to simplify screening procedures.

● Dr Elmar Joura (Medical University of Vienna, Austria) presented efficacy data on 1350 women who took part in placebo controlled trials of the anti-HPV 6,11,16,18 vaccine, Gardasil, following treatment for cervical, vulvar or vaginal pre-cancers or genital warts. These data, collected an average 1.5–1.6 years post-therapy, showed efficacy of up to 74% in preventing HPV 6/11/16/18 associated CIN, and efficacy of up to 79% for prevention of further pre-cancerous vulvar or vaginal lesions or genital warts (#366).

Dr Joura concluded that women who have been treated for cervical, vulvar or vaginal pre-cancer or genital warts, and who are therefore at increased risk of further disease, can benefit from HPV vaccination.

Supplements 'increase uterine cancer risk'

Women who take large amounts of folate, vitamin B2, B6 or B12 supplements may be increasing their risk of uterine cancer, researchers said.

A 20 year follow up of dietary intake in over 23,000 postmenopausal women in the Iowa Women's Health Study, found that women who consumed large amounts of the supplements were twice as likely to get type II uterine cancer than those with normal intakes (#669). There was no effect on type I uterine cancer.

Dr S Uccella (Mayo Clinic, Rochester, USA) explained that the results contrasted with the expected protective effects of the supplements and further investigation showed that, while a folate intake of 200–600mcg/day did have a protective effect, taking higher levels nearer 1000mcg/day increased the risk of uterine cancer.

He concluded that the research could have implications for women's health in countries such as the USA and Canada, where folate and B vitamins are added to foodstuffs.

Pregnant women 'can have cancer treatment'

Many women who discover they have cancer while pregnant risk their own health by postponing treatment. But an international collaborative study carried out in Belgium, the Netherlands and the Czech Republic, has shown that, while babies born to women who undergo cytotoxic treatment during pregnancy tend to be born prematurely and are small for gestational age, most achieve a good outcome and the incidence of congenital malformations is comparable to the general population (#1005).

The study followed 215 pregnancies in women diagnosed with invasive cancer between 1998 and 2008. Cancer treatment was started during pregnancy in 57% of cases, and it was delayed until after the birth in 27% of pregnancies. The remainder ended in spontaneous miscarriage or were terminated. Delivery was induced in 72% of pregnancies and 54% of children were born preterm.

Babies exposed to cytotoxic treatment in the womb were more likely to be born prematurely (12%, p=0.012), and to be small for gestational age children (24%, p=0.001). However, the incidence of congenital malformations was comparable to the general population.

Dr Kristel Van Calsteren (Katholieke Universiteit Leuven, Belgium) concluded that pregnancies complicated by maternal cancer have an overall satisfactory outcome, though the prevention of iatrogenic prematurity deserves attention.

Ovarian cancer 'should be treated by experts'

Women with ovarian cancer are less likely to die from their disease if they are treated by specialist gynaecological oncologists, according to a study carried out in Scotland, UK.

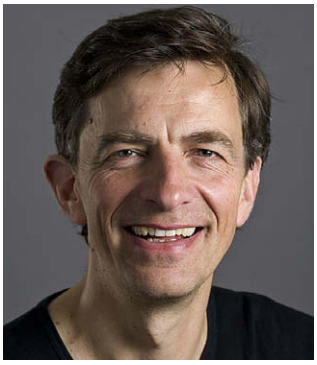
An analysis of survival data from a cohort of 912 ovarian cancer patients treated in the West of Scotland Managed Clinical Network showed a 24% lower risk of death in women treated by gynaecological oncologists who specialise in the treatment of gynaecological cancer than by general gynaecologists who treat the full range of gynaecological problems that women can experience (#1448).

Reporting her findings at a late breaking session, Dr Alex Stirling (West of Scotland Cancer Surveillance Unit) said that a recent reorganisation of cancer services in Scotland was intended to provide equal standards of care for patients wherever they lived. However, some women continue to be treated away from larger cancer centres, and do not have access to gynaecological oncologists.

Cancer services are to be centralised so that selection of cases for surgery will be decided by a specialist multidisciplinary team. This should ensure that more difficult cases are treated by gynaecological oncologists, she said.

PODIUM

Creating a healing environment



Professor Christoffer Johansen is head of the department of psychosocial research at the Danish Institute of Cancer Epidemiology, the Cancer Society, and a former President of the International Psycho Oncology Society (IPOS). He has an interest in how the aesthetics of the hospital environment interact with cancer treatment.

What aspects of the hospital environment are you concerned about?
Colours, noise, and room lighting; where treatment facilities are situated (x-ray cellars and chemo rooms are usually separate from the general social life in a hospital); but also access to outdoor areas and facilities to make your own food, enjoy a movie, play a game of pool – or just relax in the leather arm chair in the library.

Are you calling for special treatment for cancer patients?
No, this is a wider problem. The physical structures in that part of society which is meant to take care of people, who are seriously ill, are made of concrete, steel and glass. The treatment of disease is unconnected to the person and their social circumstances, and this environment further depersonalises them. It is not designed to support the care that is being offered. It lacks any charm; there are straight long corridors, square rooms, and neon lights, which operate in the green visual light frequency and make everything look ugly including the colour of patients' faces.

The underlying ideology is irrational, as if the environment has been designed for the equipment and technology it houses, not the people in it. We have apparently done everything we can to make them unfriendly, unwelcoming and cold.

Why have we developed such environments?
Following the second world war, society became fascinated by technology and technological advances. We believed we could remove disease from a person; we thought it was an objective phenomenon and for that reason we created objective depersonalised environments.

Now we don't believe disease is a 'thing'; it is the person. Cancer is a social disease. If a woman gets breast cancer, it will hit the family. Several studies have found that spouses are more distressed than patients; children are also distressed. However, this is not sufficiently acknowledged by the medical establishment. Cancer is a subjective social process which involves both the patient and most members of their family. We have to dramatically reconstruct institutions so that they truly support the healing process.

How could we be more rational?
Several studies have examined links between measurable outcomes and, for example, neon light versus natural light through windows, colours and access to green areas round hospital. They have shown benefit from consistently including measures to improve the environment within institutional buildings. However, most are observational or use historical groups as controls so that methodological problems hamper the results.

Is there an appetite for making these changes during an economic recession?
We need to start thinking about this because over the longer term – the next couple of decades – in Denmark, for example, there will be a programme of hospital reorganisation and restructuring. We will develop many new large hospitals; we are building bigger and bigger units to serve whole regions, because we can't afford to have small municipal city hospitals any longer. We need to think carefully about the environment we want to create.

Many people spend much less time in hospitals than before – is this as important as it was?
It is possible for a woman to come into a hospital at 8 o'clock for a mastectomy and to have left by 2 o'clock in the afternoon. But she will still be coming back to the hospital for chemotherapy, radiation treatment and for follow up scans. X-ray departments are often like the cellars of the institution, they're dark and uninviting and don't encourage attendance. We have to shield the x-rays, but we could create pleasant areas around the treatment facilities.

Although the majority of patients leave quite quickly, others spend a lot of time in hospital. Certain activities should be provided: a library, a fitness centre, patients' kitchens etc. – a hospital should include the things you like about where you live.

There must be cost implications?
You would have to include a comparison of the price of a patient remaining in bed or leaving hospital. A constructive environment encourages patients to get up, and in turn leave hospital earlier. We want to ease the transition from hospital to their own home; they should have access to normal daily activities in hospital, be able to cook their own food and watch their own DVDs. In this way, an improved environment could have economic benefits.

In a financial crisis, spending on beauty and the environment is always the first to be cut. But there is currently a debate about this in Denmark. The argument applies not just to hospitals – and all sectors of the health system – but also in homes for elderly people, kindergartens and schools. We have created architectural structures which don't support our interventions.

We need to conduct randomised controlled trials to find out which aspects of the environment can help patients in different situations. We need to investigate the details of this much more carefully.

Helen Saul