Detailed imaging of areas of interest on microscopic level is now possible by the use of confocal microscopes incorporated in the endoscope or in small mini probes.
Early neoplastic lesions can effectively be treated by focal removal using endoscopic mucosal resection (EMR). Until recently, the EMR-cap was the most common technique for this purpose but with multi-band mucosectomy an easier endoscopic resection technique has come available.
After focal removal of neoplastic lesions the remaining Barrett's segment remains at risk for further neoplastic progression. Additional treatment to remove this risk is therefore required. Complete endoscopic resection of the Barrett segment suffers from the high rate of the stenosis. A new endoscopic ablation technique, known as radiofrequency ablation may surpass this problem. Recent studies suggest that this technique is highly effective, not associated with severe complications, or esophageal stenosis and results in a complete endoscopic and histological removal of the whole Barrett's segment.
The combination of state of the art endoscopic imaging and these new endoscopic treatment modalities will result in the effective endoscopic management of patients with early Barrett's neoplasia and should be incorporated in guidelines as well as training programs.

Special Session (Thu, 24 Sep, 11:15−12:15)
New approaches for evidence generation of novel radiation technologies

333 INVITED

Development and assessment of novel radiation techniques – a medical physics perspective

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The medical physics community has a long and successful history in the development and advancement of novel methods for the detection and treatment of disease. These advancements are typically motivated by the desire to improve the likelihood of managing the disease and/or to minimize any therapy-induced toxicity. While this desire attracts bright young physicists, engineers, and computer scientists to the field, it is not sufficient on its own to bring about any substantive change in clinical practice. Such change needs the maturation of specific technical, physical or biological challenges that can be articulated and formulated. The development of such 'validated problem sets' is an important precursor to advancing new treatment techniques – it provides the foundation for the research and development process and assures the developments will contribute to clinical care in a meaningful way. Given the background of the medical physics community, these individuals are able to bring a wide variety of novel technologies to address the challenges. Over the past 10 years, the field of oncology has seen an explosion in the number of technological advances that are employed in the treatment of cancer – particularly in the application of radiation therapy. The role of the medical physicist in these activities is not strictly defined, but focuses on methods of reducing uncertainty, increasing conformality, and assuring safety. Furthermore, it can be anticipated that the rate of novel technology development on these topics will increase, including the development of minimally invasive surgery, robotic interventions, and the development of particle therapy. With the development of novel diagnostic or therapeutic approaches, the question of cost and benefit will and should arise. One may ask, 'What is the role of the medical physicist in this activity?" Clearly, as a functioning member of the health care profession, medical physicists have an obligation in this regard as well. This could be seen as placing the medical physicist in the potentially conflicted role of both advancing technology for the benefit of society, as well as, engaging in its broad use and evaluation. However, the medical physicist needs to rise above this simplistic presentation of a more complex conflict. The solution to this dilemma is found in our training as physicists and engineers. We must focus on the clear formulation of the problem we are seeking to address and emphasize the importance of being rigorous in our evaluation and comparison of arising technologies. In this presentation, the challenge of evaluating technological developments in radiation therapy will be discussed in an 'engineering paradigm' that can be contrasted with conventional 'evidenced-based' approaches.

Special Session (Thu, 24 Sep, 11:15−12:15)
Future trends and EONS projects

334 INVITED

Prostate cancer and supportive care: European training needs analysis

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Prostate cancer is increasing in incidence and will continue to place a significant burden on the health care systems of all developed countries. In Europe it is estimated that more than 300,000 new cases were diagnosed in 2006 and that this number will continue to rise. Approximately 20,000 men are being diagnosed with prostate cancer in the UK alone each year [1] and it is expected that over a third will die of the disease. Across Europe there are currently more than two million men living with prostate cancer and a man has a 1 in 12 lifetime risk of being diagnosed with prostate cancer as a result of clinical symptoms, signs or PSA testing [2]. It was only in 2001, however, that the European Association of Urology issued guidelines on the medical management of prostate cancer and there are still no known consensus statement of the nursing management or supportive care needs of these patients across Europe [2]. Research into the role of nursing or their training needs is also lacking although some evidence exists from the UK that men with prostate cancer feel that information and co-ordination of care could be improved [3]. The current PSA (Providing Supportive care & Advice) project has four phases:

1. To identify training priorities of oncology/urology nurses from 7 European countries (Denmark, France, Spain, Netherlands, Turkey, Sweden, Ireland and United Kingdom) using an Internet survey approach. The target is to obtain 100 responses from each country.
2. To survey a sample of junior medical staff using a similar method and compare their learning needs with those of the nurses.
3. To compare the nurses and doctors views with the expressed views of a sample of men living with prostate cancer.
4. To design and evaluate an education package on the topic of prostate cancer care in response to the findings.

This presentation will provide information on data from obtained form phase 1 and discuss the contextual challenges and benefits of this type of educational needs assessment [4]. The future role of EONS in advancing professional cancer education across Europe will also be discussed.

References

[1] Cancer-Research-UK. Facts on Cancer. London: Cancer Research UK, 2003.
[2] Aus G, Abbou CC, Bolla M, et al. EAU Guidelines on Prostate Cancer. *European Urology* 2005;48:546–551.
[3] Department-of-Health. National Survey of NHS Patients. Cancer-Analysis of themes. London: Department of Health, 2004.
[4] Kelly D, Gould D, White I. Modernising cancer & palliative care education: insights from one cancer network. *European Journal of Oncology Nursing* 2006;10.

335 INVITED

What does the future cancer workforce need to look like?

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Future cancer health services have a difficult balancing act, firstly between increasing demands for cancer care and diversity of provision; secondly between the need to respond to peoples cancer health needs during therapy but also to promote health and provide rehabilitation for the increasing number of cancer survivors. There are a number of challenges we face in developing the nursing workforce, from the increasing age of the EU population, projected shortfall in number of nurses and skills and knowledge to provide such nursing in the future diversity of cancer health care provision.
Epidemiological projections within the EU suggest that the Increasing life span of the older population will impact on cancer incidence. It is predicted that between 2008 and 2060 the population of the EU aged over 65 is projected to increase by 66.9 million. Cancer as a disease predominantly of older age is therefore likely to increase in incidence and put pressure on existing health services. Issues such as late detection of cancer in older age, toxicity differences, co morbidity and supportive care requirements mean that nurses need to be more aware of age related factors and have a broader knowledge of co morbidity. Workforce issues in the support of informal carers, as well as nurses in general and community settings will need to be addressed if we are to maintain quality cancer care. A further effect of the changing demographic is that there will also be fewer

nurses entering the workforce at present over half of the EU nursing workforce are over 45 years of age. As these staff approach retirement there needs to be sufficient numbers of younger recruits to replace them or an encouragement to entice staff to stay within the clinical setting.
The introduction of new therapies and improved survival of those diagnosed with cancer creates a longer term health care provision. The current success means that the numbers of people who have faced cancer is increasing by 2% a year requiring different ways of managing the volume of those who require future follow up, surveillance and after care. Oncology has focused on acute episodic care however these new developments require a shift to chronic illness models. Increasing complexity of treatment delivery requires broad skills from the nursing workforce and higher levels of proficiency and competence. Education is therefore fundamental in relation to increasing skills, keeping those nurses once trained and sustaining continuing professional development needs to be a future priority. Progress in recognising specialist cancer nursing across Europe is imperative for sustaining staff numbers and improving health outcomes. The importance of curriculum frameworks and standards across Europe will help in understanding the competence of cancer nurses. Part of this is through effective knowledge sharing through the exchange of good practice. Questions as to whether we can provide a workforce for future cancer care or what skill sets this workforce will require is important for us all. EONS aims to increase the visibility of the issues facing cancer nursing in the future.

Special Session (Thu, 24 Sep, 11:15−12:15)
Mouse models of cancer

336 INVITED

Identification of cancer genes and their collaborative networks by large-scale mutagenesis in tumour prone mice

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Insertional mutagenesis has proven to be a versatile tool to identify genes whose activation or inactivation can confer a selective advantage to cells in vitro or in vivo. The system has been exploited over the last 25 years successfully in the mouse to identify new oncogenes and tumor suppressor genes. With the availability of the complete mouse genome sequence and reliable PCR techniques this approach has become much more powerful. The insertional mutagenesis screen we performed to accelerate lymphomagenesis in mice illustrates this. Infection of newborn mice with replication-competent Moloney Murine Leukemia Virus gives rise to T and B cell lymphomas. The underlying mechanism is proviral activation of proto-oncogenes and inactivation of tumor suppressor genes. Retroviral insertional mutagenesis in over 1000 tumor-predisposed KO and control mice was performed. The largest specific cohort consisted of p53 and p19Arf KO mice. The resulting dataset with over 500 common insertion sites marking known and unknown proto-oncogenes, tumor suppressor genes, and microRNAs, also identified genotype-specific common insertion sites and highly significant co-occurrence of mutations and hits in tumor suppressor genes. The size of the dataset provided new information that could not have been extracted from smaller datasets collected previously, illustrating the “added value” of performing these studies on a large scale in defined genetic backgrounds. The approach is complementary to and can confirm the cancer-causing nature of genes identified by other approaches such as SNP analysis and high throughput sequencing of cancer genomes. Illustrating examples will be presented.

337 INVITED

Targeting DNA-repair deficiency in mouse models for BRCA-associated breast cancer

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Genetically engineered mouse (GEM) models of human cancer not only permit us to gain a detailed insight into the specific genetic changes that drive tumor initiation and progression [1], but also provide the tools to define the underlying mechanisms of drug response and acquired resistance. Once these processes are understood in sufficient detail it may be possible to design combination therapies that give rise to complete remissions, while at the same time eliminating remnant cells that might elicit recurrent disease.

Women carrying germline mutations in BRCA1 or BRCA2 are strongly predisposed to developing basal-like breast cancers, which frequently contain TP53 mutations. To study the role of BRCA1/2 loss-of-function in breast oncogenesis, we have generated conditional mouse models for BRCA1- and BRCA2-associated hereditary breast cancer based on combined inactivation of BRCA1/2 and p53 in epithelial tissues [2,3]. The mammary tumors that arise in our BRCA1 mouse model show strong similarity to BRCA1-associated breast cancer with respect to high tumor grade, expression of basal cell markers and high degree of genomic instability due to loss of homology-directed double-strand break (DSB) repair [3]. This model may therefore be helpful in predicting chemotherapeutic responses of human BRCA1-associated and BRCA1-like tumors. Indeed, preclinical intervention studies with conventional and targeted chemotherapeutics showed a selective sensitivity of BRCA1-deficient mouse mammary tumors towards agents that directly or indirectly cause DSBs, such as platinum drugs [4] or PARP inhibitors [5]. Treatment of tumor-bearing mice with the clinical PARP inhibitor olaparib (AZD2281) inhibited tumor growth without signs of toxicity, resulting in strongly increased survival. However, long-term treatment with olaparib resulted in the development of drug resistance, caused by up-regulation of P-glycoprotein drug efflux pumps. Indeed, acquired resistance could be effectively reversed by co-administration of olaparib and the P-glycoprotein inhibitor tariquidar.
BRCA1-deficient mouse mammary tumors become resistant to all drugs tested, with one exception: platinum-based chemotherapy drugs. Although tumors cannot be eradicated with cisplatin or carboplatin, the tumor recurrences invariably remain sensitive to retreatment with these drugs. These results data suggest that (partial) BRCA1 activity is required for induction of platinum resistance. Indeed, it has been reported that BRCA-associated hereditary ovarian cancers may become resistant to carboplatin by acquiring genetic reversion mutations in BRCA1/2, resulting in re-expression of BRCA1/2 and re-activation of homology-directed DSB repair [6,7]. In the mouse mammary tumors BRCA1 is inactivated by a large deletion in the Brca1 gene that cannot be reversed by any secondary mutation. To model chemotherapy resistance by genetic reversion, we have generated novel BRCA1-deficient mouse mammary tumor models mimicking defined human BRCA1 founder mutations (185-delAG and 5382-insC).

References

[1] Jonkers and Berns., Nat Rev Cancer 2002; 2:251−65.
[2] Jonkers et al., Nat Genet 2001; 29:418−25.
[3] Liu et al., Proc Natl Acad Sci USA 2007; 104:12111−6.
[4] Rottenberg et al. Proc Natl Acad Sci USA 2007; 104:12117−22.
[5] Rottenberg et al., Proc Natl Acad Sci USA 2008; 105:17079−84.
[6] Edwards et al., Nature. 2008; 451:1111−5.
[7] Sakai et al., Nature. 2008; 451:1116−20.

Special Session (Thu, 24 Sep, 11:15−12:15)
Clinical implications of new discoveries in cancer genetics

338 INVITED

Genetic susceptibility to breast cancer – new developments and clinical application

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Common cancers exhibit familial aggregation, consistent with substantial variation in inherited susceptibility. Over the past 25 years, the underlying genetic basis for this susceptibility has become increasingly understood. Three important classes of genetic loci have been identified: “high-penetrance” genes, such as *BRCA1* and *BRCA2*; “intermediate-penetrance” genes, such as *ATM* and *CHEK2*, in which mutations confer 2−3 fold risks; and “low-penetrance” loci (such as *FGFR2*), in which common polymorphisms confer more moderate risks, typically <1.5 fold. The high-penetrance loci are central in genetic counselling, but most genetic variation is explained by lower risk loci. While most if not all the important high-penetrance loci have been identified, identification of lower penetrance loci through genome-wide association studies is still in its infancy, and more further loci should be identifiable through genome scans and resequencing. Generally, genetic loci combine multiplicatively, consistent with multiple independent pathways.
Recent genome-wide association association studies have identified thirteen genetic loci with common susceptibility alleles. These loci include several plausible candidate genes, including *FGFR2*, *TNRC9*, *MAP3K1*, *LSP1* and *NEK10*, but also “gene deserts”. For the most part, the loci were not previously suspected to be related to carcinogenesis, and point to new disease mechanisms. While the risks conferred by the susceptibility