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Summary: Concept, Rationale, Evidence and Future Directions

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Introduction: Concept & rationale The concept of PBI is that radiotherapy confined to the vicinity of the primary tumour after local excision of early stage breast cancer is expected to cause fewer late adverse effects (AE) and be no less effective as whole breast radiotherapy (WBRT) for a large subpopulation of women with early breast cancer. The concept is based on the spatial pattern of local relapse (LR) after breast conservation surgery +/− WBRT. Clinical observations confirm that the majority of LR present in the vicinity of the primary tumour within the first 5 years. A minority present in other quadrants and these tend to occur over a longer time period. It is widely believed that a high proportion of other quadrant LR represent new primary tumours, not true recurrences. Which are not prevented by WBRT. It is against this background that techniques of PBI have been developed and tested.
Summary: Evidence & future directions Notable departures from conventional radiation dose-time, volume and other radiobiological parameters have been highlighted by Dr Petersen, and the relative advantages of diverse external beam and brachytherapy techniques have been presented by Drs Orrechia and Dr Van Limbergen, respectively. A summary of the evidence might go something like this. There is a large body of non-randomised evidence showing that PBI can be both safe and effective, and published consensus guidelines have described patient categories that might be suitable for different PBI approaches. Consensus indicates agreement. We may all agree, but still be wrong, an inevitable risk when mature outcome data from randomised trials are so limited. It is noticeable that LR rates in published trials of breast conservation therapies have fallen over the last 20 years, so it may not be justified to attribute very favourable outcome data in non-randomised studies to the efficacy of PBI. The future needs to avoid an environment in which the requirement for high levels of evidence is over-ridden by professional and commercial competition. Innovation often challenges the status quo, but certain principles that are abandoned at our peril.

Scientific Symposium (Tue, 27 Sep, 09:00−11:00) **Transitions in Care for Cancer Patients**

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Who are the Carers in Ambulatory Care?

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Improvements in supportive care have led to an increasing utilisation of the ambulatory care setting for patients receiving cancer treatments. Even in the more traditional surgical oncology fields, growing interest in “fast track surgery” options is leading to shorter inpatient hospital stays. Research to date has primarily focused on the physical and economical benefits of these changes in the delivery of cancer care. Less commonly discussed is the impact of this shifting responsibility for ongoing care and support from the inpatient and specialist cancer centre to the community setting. This paper will examine the research in this field and identify gaps in our current knowldege of the impact of cancer patients and their family. Alternative models for ambulatory care and sharing care responsibilities will be examined, including recent research being undertaken by the author and colleagues.

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Cultural Aspects in the Transition From Hospital to Community Care

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Background: This study examines the care transition experience of minority cancer patients and assesses barriers to effective transitions.
Materials and Methods: Qualitative and quantitative methods were used. Qualitatively − focus groups and in-depth personal interviews were conducted with patients and their families (a total of 25 patients) and with 33 providers (physicians, nurses, social workers, and administrative managers), at hospital and community settings. The quantitative phase included administration of a validated questionnaire − the Care Transition Measure (CTM), that rates patients' care transition experience on a 0−100 point scale; and structured observations on the hospital discharge process (on the explanations provided and the language used during the discharge briefing). Participants were adult oncology patients at a large Oncology Center in Israel, who speak Hebrew, Arabic or Russian, to reflect the majority and two of the largest minority spoken languages in Israel.
Results: Qualitative analysis showed that patients face a complex and fragmented system with multiple providers and services. Difficulties in navigating the health care system are exacerbated for minorities with language and cultural barriers. Mechanisms to overcome barriers include undertaking of informal care coordinating roles by the patients' general practitioners (GPs) or nurses. The quantitative phase included a survey of 422 patients. GPs who treated Arabic and Russian speaking patients were more likely to discuss the discharge recommendations with their patients than physicians who treated Hebrew speaking patients. GPs' involvement was found to be the most significant variable affecting the quality of the transition process as rated on the CTM ($p < 0.001$). Structured observations on the discharge process of 62 minority patients showed that provider-patient language concordance was one of the strongest correlates of effective care transitions ($p < 0.001$).
Conclusions: Our findings point to the role of interpersonal care, including discussion of hospital care transition recommendations with the GP and in-hospital provider-patient language concordance, in promoting effective care transitions. Interventions targeted towards care transition support for minority patients should emphasize ongoing counseling throughout the care trajectory (during and post hospitalization).

370 INVITED

Transition to Survivorship: Key Issues and Models of Care

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Due to advancements in diagnosis and treatment, the number of cancer survivors is increasing dramatically across the globe. To assure the highest quality of life for these individuals, new models of care are being developed, implemented and evaluated. This session will examine the most important issues facing survivors and describe the new, efficient models of care that are focused on the provision of comprehensive services to address them − surveillance for recurrence; screening for second cancers; prevention, surveillance and intervention for long term and late effects; health promotion counseling; psychosocial services and communication between specialist and generalist providers. Novel practice settings and new provider models will be discussed, as well as recommendations for program metrics and needed empirical evaluations of these new approaches to providing survivorship care.

371 INVITED

Facilitating Transition to Palliative Care

Abstract not received

Scientific Symposium (Tue, 27 Sep, 09:00−11:00) **Hepatocellular Carcinoma: Novel Advancements in Diagnosis and Treatment**

372 INVITED

New Molecular Targeted Therapies

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Hepatocellular carcinoma (HCC) has increased its mortality in the US and Europe in the last decades. Since most patients are still diagnosed at advanced stages, there is an urgent clinical need for developing novel systemic agents. In this setting, sorafenib, a tyrosine kinase inhibitor (TKI) with blockade activity against BRAF, VEGFR and PDGFR, has demonstrated its antitumour activity by significantly improving survival of patients with advanced HCC. This major advancement has paved the way for exploring novel molecular agents and combination of drugs in this complex disease.
There is a blossom of high-end pivotal trials for regulatory approval in HCC research. These studies mostly test TKI in combination (e.g., erlotinib) or in comparison (e.g., linifanib, brivanib) with sorafenib in first line. In addition, for patients failing or intolerant to sorafenib, new trials are testing TKI (e.g., everolimus, brivanib) and monoclonal antibodies (e.g., ramucirumab) in second line. Early clinical trials are also exploring signals of efficacy for up to 60 novel drugs in the field. All these studies might change the management of patients by 2012–2014 in an unprecedented manner, and can establish the *backbone* combination therapy to be applied to

all advanced cases. It is also expected that as a result of identification of oncogenic addition loops, biomarker-based trial enrichment will be the mainstay to progress in this field towards a more personalized approach. Drugs blocking key drivers will be added to backbone therapies in selected populations to maximize the efficacy and cost-benefit of these otherwise expensive interventions.

373 INVITED

Novel Imaging Techniques and Treatment Assessment for Evaluating Benefit From Targeted Agents

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Sorafenib, a tyrosine kinase inhibitor, has shown clinical efficacy in patients with hepatocellular carcinoma (HCC) and is the standard of care for patients with advanced-stage HCC. Nowadays, many targeted therapies are evaluated in HCC either as sole treatment or in combination with other treatments such as tumour ablation, chemo-embolization, and surgical resection. Therefore, there is a need to assess efficacy of targeted therapy in HCC.
RECIST is the reference method to evaluate treatment efficacy in soild tumours but does not seem appropriate in evaluating targeted therapy as objective responses were seen in very few cases in patients treated with sorafenib or sunitinib.
New criteria have been proposed to evaluate treatment efficacy of non surgical treatments in patients with HCC. The most common ones are the Choi criteria, the EASL criteria, and the modified RECIST criteria. All these criteria mainly focus on internal tumour changes such as appearance of necrosis or disappearance of tumour hypervascularity. Many examples will be shown during the lecture.
Another approach is based on functional imaging and especially perfusion-related imaging. Contrast-enhanced ultrasound, CT perfusion and dynamic contrast-enhanced MR imaging have the capability to assess perfusion changes in patients under treatment. Advantages and disadvantages of these modalities will be discussed.
Last, other functional tools that are not routinely used will be presented.

374 INVITED

Local Therapy for HCC

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The management of hepatic tumours, is becoming an increasingly significant problem. Hepatocellular carcinoma (HCC) (and colorectal cancer (CRC)) are among the five most common causes of cancer deaths worldwide. The incidence of HCC is increasing, linked with hepatitis B and C. An increase in the incidence of cholangiocarcinoma (CC) has also been reported. For several years, surgical resection has been the standard treatment for HCC. Unfortunately, the majority of patients with hepatobiliary tumours or HCC are inoperable, either because of impaired liver function, central location of the tumour, or comorbid illness. For these patients, other techniques have been developed and evaluated such as liver transplantation, systemic chemotherapy, intra-arterial hepatic chemoembolization, immunotherapy, destruction by radiofrequency, cryotherapy, and laser thermotherapy. Currently, the exact indication for each of these different treatment modalities has not been defined, and there is no standard treatment for inoperable hepatic tumours. Radiotherapy, alone or combined with chemotherapy, has become an additional treatment option.
Stereotactic body radiation therapy (SBRT) for liver disease has been reported with encouraging rates of local control and toxicity. Unfortunately, the published series are heterogeneous for the doses used as well as the number of patients treated, and so do not permit reliable univariate or multivariate analyses. A review of different techniques will be presented.

375 INVITED

Liver Transplantation and Resection for HCC

Abstract not received

Scientific Symposium (Tue, 27 Sep, 09:00–11:00)
From Bench to Bedside in Ovarian Cancer

376 INVITED

New Concepts on the Origins of Ovarian Cancer

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Epithelial ovarian tumours are heterogeneous neoplasms which are classified according to cell type into serous, mucinous, endometrioid, clear cell, transitional, and squamous cell tumours. Parenthetically, none of these cells are found in the normal ovary and the development of different tumour cells has long been attributed to mullerian "neometaplasia" of the ovarian surface epithelium (mesothelium). More importantly, these tumours are further subdivided into benign, borderline (intermediate), and malignant (carcinoma) depending upon the degree of cell proliferation and nuclear atypia, and the presence or absence of stromal invasion.
Malignant epithelial tumours (carcinomas) are the most common ovarian cancers, accounting for 90% of cases, and are the most lethal gynecological malignancies. Currently, based on light microscopy and molecular genetics, ovarian carcinomas are subdivided into at least five main subtypes: high-grade serous carcinomas (70%), endometrioid carcinomas (10%), clear cell carcinomas (10%), mucinous carcinomas (5%), and low-grade serous carcinomas (<5%) (Table). These tumours account for 98% of ovarian carcinomas, can be reproducibly diagnosed, and are inherently different diseases, as indicated by differences in epidemiological and genetic risk factors, precursor lesions, patterns of spread, molecular events during oncogenesis, response to chemotherapy, and outcome.
Recent evidence suggests that what have been traditionally thought to be primary ovarian cancers actually originate in other pelvic organs and involve the ovary secondarily. In fact, it has been proposed that high-grade serous carcinomas arise from precursor epithelial lesions in the distal fimbriated of the fallopian tube, whereas endometrioid and clear cell carcinomas originate from ovarian endometriosis.

Table: Ovarian carcinoma: clinical and molecular features of the 5 most common subtypes

	HGSC	LGSC	MC	EC	CCC
Risk factors	BRCA1/2	?	?	HNPCC*	?
Precursor lesions	Tubal intraepithelial carcinoma	Serous borderline tumour	cystadenoma/ borderline tumour?	Endometriosis	Endometriosis
Pattern of spread	Very early transcoelomic spread	Transcoelomic spread	Usually confined to ovary	Usually confined to pelvis	Usually confined to pelvis
Molecular abnormalities	BRCA, p53	BRAF, KRAS	KRAS, HER2	PTEN	HNF1
Chemosensitivity	High	Intermediate	Low	High	Low
Prognosis	Poor	Intermediate	Favorable	Favorable	Intermediate

*Hereditary non-polyposis colorectal carcinoma.

377 INVITED

Genomics of Ovarian Cancer – Utility as Predictive Biomarkers

Abstract not received

378 INVITED

New Directions in Angiogenesis Therapy

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Ovarian cancer accounts for thousands of lives each year and new treatments are needed. Although surgery and chemotherapy are effective cytoreductive strategies, maintenance therapy had proved elusive until recent data on anti-angiogenic agents emerged. Two trials, GOG218 and ICON7, have tested the benefit of adding bevacizumab, an anti-Vascular Endothelial Growth Factor (VEGF) antibody to carboplatin and paclitaxel. The trials demonstrated that in patients with bulk residual FIGO stage III/IV disease, progression free survival (PFS) was increased by approximately 6 months in the experimental arms. Overall survival (OS) data for ICON7, presented recently, reported an 8-month OS advantage in high-risk patients on the experimental arm.
GOG218, which incorporated doses of bevacizumab that were twice those used in ICON7, has not yet reported an OS difference, although mature data are not yet available. The reason for the apparent difference in survival between the two trials is unknown but may be due to the more widespread use of VEGF inhibitors in the control arm after progression in GOG218. Evidence to support the hypothesis that bevacizumab is active in recurrent disease emerged in the recently presented OCEANS trial, which demonstrated that bevacizumab improves PFS by 4 months