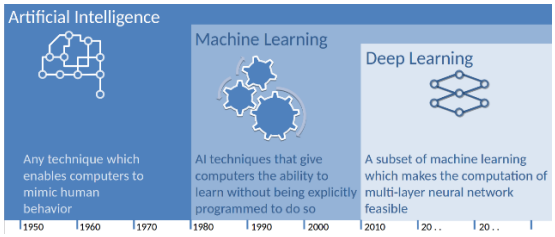
ESTRO 38 Saturday 27 April

Teaching Lecture: Artificial Intelligence Applications in Radiation Oncology

SP-0001 Artificial Intelligence Applications in Radiation Oncology

N. Dinapoli[1], J. Lenkowicz[2], C. Masciocchi[2], A. Damiani[2], l. Boldrini[2], d. Cusumano[3], v. Valentini[1]
[1]*Fondazione Policlinico Universitario A. Gemelli IRCCS, UOC Radioterapia Oncologica- Dipartimento di Diagnostica per immagini- Radioterapia Oncologica ed Ematologia, Roma, Italy ;* [2]*Università Cattolica del Sacro Cuore, Dipartimento di Diagnostica per immagini- Radioterapia Oncologica ed Ematologia, Roma ,Italy;* [3]*Fondazione Policlinico Universitario A. Gemelli IRCCS, UOC Fisica Sanitaria- Dipartimento di Diagnostica per immagini- Radioterapia Oncologica ed Ematologia,Roma, Italy*

Abstract text
Artificial intelligence (AI) is a very generic concept defined as "*the study of agents that receive percepts from the environment and perform actions*" (S. Russell). It is being developed by using information technology, software and hardware, designed to create functions and procedures oriented to *learn* from, and process, data. First experiences of AI started from the beginning of computer age but thanks to the availability of high performance computing hardware (like GPUs or cloud computing) nowadays AI is booming in many fields of business, technology, e-commerce and, last but not least, health and medicine. What are the main tools available for creating AI based models in medicine? In a simplified slide published on Oracle® website (https://blogs.oracle.com/bigdata/difference-ai-machine-learning-deep-learning, Figure 1)



AI world includes applications as Machine Learning (ML), a part of which is constituted by so called Deep Learning (DL). In radiation oncology there are already many potential application of AI, ML and DL, being the number of the last ones increasing, step by step, in last years. For example, fields of application of AI can be the automatic target or organs at risk delineation process, the auto-planning procedures or different modeling processes of patients evaluation and prognosis. In literature there are several examples of AI applications, but a first summary of them needs to understand how AI algorithms can work and be applied to daily workflow, like DL and its use in imaging related applications. The complexity and extraordinary fast evolution of DL based applications seems to prelude the possibility of more and more self automated clinical workflows, starting from treatment prescription aids, going through volumes delineation and finally managing the whole treatment delivery process, both taking into account imaging (IGRT) based and clinical issue for toxicity management. Clinical and concurrent ethical issues will raise as soon as AI based applications will offer in medicine, and radiation oncology, a sufficient grade of automation, likewise the self-driving car are provoking ethical discussions about how to proceed in case of accidents and damages to the human beings.

Teaching Lecture: Using mice to model normal tissue responses to thoracic radiation

SP-0002 Using mice to model normal tissue responses to thoracic radiation

Andy Ryan[1]
[1]*Oxford University, Oncology, Oxford, United Kingdom*

Abstract text
Thoracic radiotherapy is widely used for the treatment of cancer, with either curative or palliative intent depending on the stage of the disease. Radiation dose is limited by normal tissue effects where common side effects include oesophagitis, pneumonitis and pulmonary fibrosis. As new approaches to improving the effectiveness of radiation enter clinical trials, a key challenge to the field is to understand the potential impact of new agents on the therapeutic ratio in patients. Using PARP, ATR and ATM inhibitors as exemplars, the effects of radiation combination therapy will be described in established models of toxicity (C57BL/6 mice) and efficacy (subcutaneous xenografts grown in BALB/c nude mice). Recently, we have developed a new in vivo approach with the potential to evaluate both toxicity and efficacy in a single mouse model. A/J mice are treated with urethane which leads to the development of lung tumours over a period of 6-9 months. In this model, radiation treatment has significant anti-tumour effects, but also induces pneumonitis and fibrosis. Using this new model , we outline emerging data using PARP, ATR and ATM inhibitors in combination with localised radiation, and suggest this may be a better approach to determining the potential impact of new agents on the therapeutic index of radiation therapy.

Teaching Lecture State of the art in definitive treatment of locally advanced NSCLC

SP-0003 State of the art in definitive treatment of locally advanced NSCLC

C. Faivre-Finn[1]
[1]*The Christie NHS Foundation Trust, Division of Cancer Sciences -Radiation Oncology, Manchester, United Kingdom*

Abstract text
Approximately one third of patients with non-small cell lung cancer (NSCLC) present with stage III disease and the majority of these patients are inoperable. Treatment of inoperable stage III NSCLC requires both control of the local disease and the distant micrometastases. The international standard of care is concurrent chemo-radiotherapy (CTRT) that is associated with a 5 year survival rate of 20-25% (Auperin, Ramnath, Eberhardt). The literature supports the use of concurrent CTRT, in selected patients with good performance status, without major co-morbidities and for whom the RT plan produces acceptable normal tissue doses. Data in the elderly population is limited. The addition of chemotherapy concurrently to RT increases the risk of severe oesophagitis but does not increase the risk of lung toxicity. To date there is no established standard concurrent CTRT regimen in Europe. Neither the addition of induction or consolidation CT to concurrent CTRT have led to improvements in survival in unresectable locally advanced NSCLC. There is no role for dose escalation in stage III NSCLC using conventional dose fractionation

(Bradley).
Major progress has been made in recent years in the field of radiotherapy planning/delivery (i.e. 4DCT, PETCT, IMRT and VMAT) and treatment verification (daily on-line cone beam CT).
For the majority of patients, concurrent CTRT is not suitable due to performance status and co-morbidities. The alternative treatment options are chemotherapy followed by RT (sequential CTRT), or RT alone. The latter is associated with a 5 year survival rate of less than 10 %, due to both locoregional and distant relapse. There is currently no established role for induction, consolidation chemotherapy or targeted agents in stage III NSCLC. The PACIFIC trial has recently established a new standard of care by shown ing a progression-free and overall survival advantage for consolidation immune check-point inhibitor (Antonia).
PCI in stage III NSCLC reduces the incidence of brain metastases but has not been demonstrated to reduce survival in the reported studies (Paumier). The role of post-operative RT in completely resected patients with N2 disease is controversial (Le Péchoux).
Aupérin A et al. Meta-analysis of concomitant versus sequential radiochemotherapy in locally advanced non-small-cell lung cancer. J Clin Oncol. 2010; 28(13):2181-90.
Ramnath N, et al. Treatment of stage III non-small cell lung cancer: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2013;143(5 Suppl):e314S-40S
Eberhardt WE etal. 2nd ESMO Consensus Conference in Lung Cancer: locally advanced stage III non-small-cell lung cancer. Ann Oncol. 2015 Aug;26(8):1573-88.
Bradley J, et al. Standard-dose versus high-dose conformal radiotherapy with concurrent and consolidation carboplatin plus paclitaxel with or without cetuximab for patients with stage IIIA or IIIB non-small-cell lung cancer (RTOG 0617): a randomised, two-by-two factorial phase 3 study. Lancet Oncol. 2015;16(2):187-99
Paumier A, et al. Prophylactic cranial irradiation in lung cancer. Cancer Treat Rev. 2011 Antonia SJ ,et al. Durvalumab after Chemoradiotherapy in Stage III Non-Small-Cell Lung Cancer. N Engl J Med 2017 ;377(20):1919-1929.
Antonia SJ, et al. Overall Survival with Durvalumab after Chemoradiotherapy in Stage III NSCLC. N Engl J Med. 2018 Sep 25
Le Péchoux C.Role of postoperative radiotherapy in resected non-small cell lung cancer: a reassessment based on new data. Oncologist. 2011;16(5):672-81

Teaching Lecture: New ILROG radiotherapy guidelines for haematological malignancies

SP-0004 New ILROG radiotherapy guidelines for haematological malignancies

L. Specht[1]
[1]The Finsen Center - Rigshospitalet, Oncology, Copenhagen, Denmark

Abstract text

The International Lymphoma Radiation Oncology Group (ILROG) is a worldwide organization of radiation oncologists interested in lymphomas and other haematological malignancies. Our goal is to improve outcome for patients by encouraging the appropriate integration of radiation therapy (RT) in the management of these diseases. One of the most important tasks has been to develop and teach the use of modern, image-guided and highly conformal RT for the many different disease entities and anatomic distributions.
A very important task has been the development and publication of guidelines. In 2014-15 we published ILROG guidelines on the treatment of Hodgkin lymphoma, pediatric Hodgkin lymphoma, nodal non-Hodgkin lymphoma, extranodal lymphomas, and primary cutaneous lymphomas. They proved very popular, being some of the most frequently downloaded publications in radiation oncology. In 2017 we gathered in Boston with the aim of defining other areas where guidelines were needed. We have subsequently published 9 new guidelines covering the following areas:
Relapsed or refractory Hodgkin lymphoma, where RT has long been demonstrated to be a powerful agent in the local control. It may even be effective when used alone in selected cases. Many patients undergo high-dose chemotherapy (HDCT) and stem cell transplant (SCT), but they frequently relapse in sites of prior disease, and this risk is reduced in patients treated with RT. The indications for RT in these patients are: 1) localized relapse, 2) disseminated relapse but with either bulky disease, persistent FDG-avid disease, or involvement of areas considered critical for local control. It is debated whether the RT should be given before or after the SCT. The doses and volumes depend on the response to chemotherapy and the extent of disease.
Relapsed/refractory diffuse large B-cell lymphoma, where RT may also provide effective local control. Young patients without comorbidities and with chemosensitive disease are often offered HDCT and SCT, and RT is used according to the same principles as for Hodgkin lymphoma. For patients who are not eligible for transplant, RT can offer effective palliation and for patients with locoregionally confined disease even cure. Doses vary according to the response to chemotherapy, and may in refractory disease go as high as 45-50 Gy. Volumes depend on disease location and extent.

Solitary plasmacytoma are potentially curable with RT. Doses vary from 35 Gy to small lesions to 40-50 Gy to large lesions. For patients with multiple myeloma RT is an effective palliative treatment at lower doses.
Total body irradiation (TBI) continues to be an important part of conditioning regimens for allogeneic SCT. Many different techniques have been used, most often at extended source-to-skin distance (SSD). Increasingly, 3-dimensional planning and intensity modulated therapy are being used. This may allow reductions of the doses to risk organs. With some of these techniques the TBI is no longer delivered simultaneously to the entire body, possibly leading to some circulating leukemia cells receiving reduced doses. The TBI may be delivered at standard SSDs leading to higher dose rates, which has the potential to increase toxicity.
Extramedullary leukemia can pose therapeutic challenges for which RT can have an important role. RT should be considered for isolated chloromas with inadequate response to chemotherapy, for isolated recurrences after SCT, and for palliation. Leukemia cutis may be treated with electron therapy, if large areas are involved total skin electron beam therapy may be used. A dose of 24 Gy results in excellent, rapid, and durable local control.
Central nervous system leukemia may be an indication for RT, in particular in patients with recurrent or refractory CNS leukemia. Whole brain RT is usually given at doses of 24 Gy, but for selected patients treated with curative intent, cranio-spinal RT may be indicated.
Lymphoblastic lymphoma with a large mediastinal mass often relapse in the mediastinum after treatment with intensive chemotherapy. Mediastinal RT can improve local control, but toxicity is a concern.
Proton therapy for mediastinal lymphoma may help to reduce the radiation dose to the normal structures thereby reducing long-term toxicity. There are many uncertainties in proton therapy, and these need to be considered.
Imaging with FDG-PET plays a major role in the treatment planning of many lymphoma types. Accurate definition of sites of involvement before any systemic therapy is