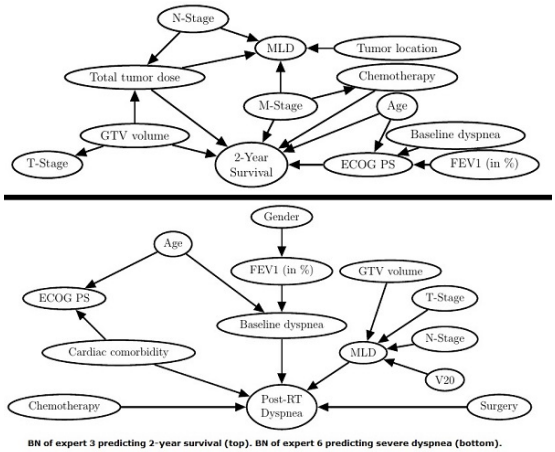
Results: Expert networks were more complex with up to 30 arcs while the data-driven algorithm selected no more than 6 arcs. Expert and data-driven models were not significantly different in discriminative ability (see 95% confidence intervals in table). Further, AUCs of all models except expert 6 were not significantly different from 0.5. Patients with 2-year survival could be discriminated better as it was significantly different from chance in 4 expert models and the data-driven model. The data-driven model was significantly better than two expert models.
Conclusions: Discrimination of patients with 2-year survival after lung RT is achievable with both methodologies – expert-based and data-driven models. Reliable discrimination of patients with severe dyspnea after RT is not achievable with the presented models learned on data of 792 patients. Neither expert-based or data-driven models outperform each other. Thus, there is dire need for biomarkers predictive of radiation-induced dyspnea. For both endpoints, the algorithmically derived models are more parsimonious and perform as well as the expert-based models or better.

		Predicting Severe Dyspnea (CTCAE dyspnea scores ≥2)				2-Year Survival			
		AUC	AUC 95%CI	(AUC - $AUC_{Alg.}$) 95% CI	# Arcs	AUC	AUC 95%CI	(AUC - $AUC_{Alg.}$) 95% CI	# Arcs
Expert	1	0.58	[0.42,0.73]	[-0.07,0.22]	30	0.59	[0.48,0.7]	[-0.27,0.01]	19
	2	0.61	[0.43,0.77]	[-0.14,0.32]	9	0.65	[0.54,0.76]	[-0.21,0.07]	15
	3	0.49	[0.32,0.65]	[-0.19,0.15]	23	0.69	[0.58,0.8]	[-0.13,0.1]	17
	4	0.59	[0.45,0.73]	[-0.06,0.22]	22	0.56	[0.44,0.68]	[-0.32,-0.01]	23
	5	0.65	[0.5,0.8]	[-0.05,0.32]	20	0.53	[0.4,0.65]	[-0.36,-0.01]	13
	6	0.69	[0.56,0.83]	[-0.03,0.39]	14	0.64	[0.53,0.75]	[-0.21,0.05]	16
	7	0.57	[0.43,0.7]	[-0.08,0.2]	7	0.68	[0.57,0.79]	[-0.19,0.12]	20
Alg.		0.52	[0.38,0.66]	[0,0]	6	0.72	[0.6,0.82]	[0,0]	4



BN of expert 3 predicting 2-year survival (top). BN of expert 6 predicting severe dyspnea (bottom).

Keywords: personalized radiotherapy, Bayesian prediction modelling

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Proton Radiation Therapy: Current Status at Massachusetts General Hospital
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Purpose: Because of the absence of exit dose beyond the Bragg peak, protons can improve the radiotherapy physical dose distribution. This offers the potential for dose escalation to improve local control in anatomic sites and histologies where local control of tumor is suboptimal with photons. At the same time, the reduction in the normal tissue dose/volume profile is anticipated to reduce acute and late normal tissue toxicity. The competing technologies include intensity modulated photon radiation therapy (IMRT) as well as heavier charged particles. Massachusetts General Hospital (MGH) has been a pioneer in the development of proton radiation therapy. An overview of the proton radiation therapy program at MGH will be provided which will illustrate technological progress in proton therapy.
Materials/Methods: The initial treatment facility was in the Harvard Cyclotron Laboratory, a physics laboratory which was modified to accommodate patient treatments. Beam generated in a 160 MeV cyclotron was delivered via fixed horizontal beams. In 2001, the program was moved to a dedicated clinical facility based at the hospital, the Francis H. Burr Proton Therapy Center (FHBPTC). In 2017, an additional single room, gantry-based treatment facility will open.
Results: The FHBPTC has a 230 MeV cyclotron delivering beam to two rooms equipped with 360-degree rotational gantries and a third clinical room with a two beam-lines, one dedicated for treatment of eye tumors and the other for stereotactic intracranial radiosurgery/radiotherapy. In 2014, we delivered 13, 370 patient treatments at the FHBPTC. Currently, one of the two gantries delivers scanned proton beams including intensity modulated proton therapy. The other gantry delivers passively scattered proton treatments. We have U.S. National Cancer Institute funding to support clinical trials of intensity modulated proton therapy and to study the clinical impact of differences between proton and photon dose distributions, to optimize IMPT delivery including robust optimization, and to study proton dose perturbations caused by the heterogeneous patient and inter- and intra-factional variations. We are also active participants in ongoing NRG Oncology proton clinical trials.
Conclusions: Proton radiation therapy offers a number of potential treatment advantages to patients over photons related primarily to differences in physical dose distribution; clinical gain can be assessed in clinical trials which are currently in progress. Rapid changes in technology must be considered in designing and conducting clinical trials in this area.

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Macrophage reprogramming for anticancer therapy
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Tumor-associated macrophages (TAMs) are a phenotypically and functionally heterogeneous assortment of monocyte-derived cells that participate to key processes associated with tumor progression, such as angiogenesis, immunosuppression, invasion, and metastasis. Increasing studies also show that TAMs can either enhance or antagonize the antitumor efficacy of cytotoxic chemotherapy, cancer-cell targeting antibodies, and immunotherapeutic agents, depending on the tumor type, macrophage activation state, or type of treatment. TAMs can also drive reparative mechanisms in tumors after radiotherapy or treatment with antiangiogenic drugs. At the meeting, I will discuss the biological significance and clinical implications of these findings, with an emphasis on novel approaches, based on microRNA (miRNA) targeting, to reprogram TAMs into immunostimulatory cells. Indeed, we found that efficient miRNA depletion in TAMs did not alter their abundance in the tumors, but markedly reprogrammed their transcriptomes and effector functions from immunosuppressive to immunostimulatory. This enhanced cytotoxic T-cell infiltration, abated tumor progression, and increased tumor responsiveness to immune checkpoint blockade. Bioinformatics analysis of TAM transcriptomes identified a limited set of miRNAs putatively involved in TAM programming, and re-expression of Let-7 in Dicer-deficient TAMs was sufficient to rescue TAM's protumoral phenotype and abate tumor CTL infiltration. Collectively, these results have identified a mechanism of TAM programming to an immunostimulatory phenotype that may be exploited to enhance the efficacy of cancer immunotherapies.

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The search for genetic predictors of radiotherapy response

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The aim of radiotherapy is to eradicate cancer, while at the same time minimizing the side effects. Although important improvements in imaging and radiotherapy techniques have enabled better target definitions and radiotherapy delivery, normal tissues are always exposed to radiation to some degree. Side effects thus still occur, but their variable degree, even when corrected for dosimetric characteristics, suggests that common genetic variants may play a role. However, similar to other human traits, radiosensitivity is considered to be a complex polygenic phenotype determined by the interaction of multiple loci.
Identifying these genetic markers will further enable precision radiotherapy in which the optimal treatment plan will take into account the genetic pre-disposition to toxicity (and of the tumour). It should not be assumed that all of the phenotypic variation is due to germ line genetic variation, but that that epigenetic changes (inherited and acquired) could also be important, including variants in mitochondrial DNA.
In response to the lack of success of candidate gene SNP studies in small studies, the focus of radiogenomics has shifted towards GWAS and big data research within international networks (1). At the same time, effort was made to establish standardized methods for reporting on radiogenomics (2). In recent years, remarkable progress has been made in the field of radiogenomics, of which some examples are cited.
Single nucleotide polymorphism genotypes were determined in female breast cancer patients from the RAPPER study, showing that patients with a high polygenic predisposition to breast cancer do not have an increased risk of radiotherapy toxicity, but that individual variants may increase risk (3). Identifying SNPs in oxidative stress-related genes associated with risk of late toxicities in breast cancer patients receiving radiation therapy, a variant allele in the base excision repair gene XRCC1 was found that could be used in combination with additional variants to predict late toxicities (4).
A GWAS study in 1742 prostate cancer patients treated with external beam radiotherapy identified the TANC1 locus (that has a role in regenerating damaged muscle) to be of significant importance in the development of late radiation-induced damage (5). It is expected that these and other improvements in genotyping together with better phenotyping of patients will be incorporated in treatment planning, decision support systems and drug development to increase the therapeutic ratio of radiotherapy.

Keywords: radiogenomics, side effects

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Combinaison of an anti HPV-E7 vaccine to radiotherapy: preclinical data in a head and neck model.

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Combinaison of radiotherapy and immunomodulatory approaches is an emerging field. Beside the concurrent inhibition of immune checkpoints inhibitors, the association of anti tumor vaccines is a way to stimulate specific anti tumor immunity during radiotherapy. Here, we report an extremely effective combination of local irradiation (IR) and Shiga Toxin B (STxB)-based human papillomavirus (HPV) vaccination for the treatment