Virtual 5 x 5 Symposium

Will all radiotherapy be delivered in maximum 5 fractions?

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DEGRO AKADEMIE

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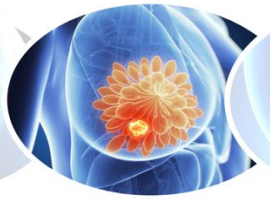
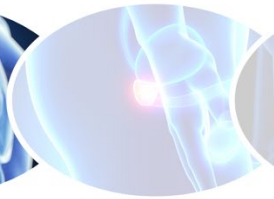
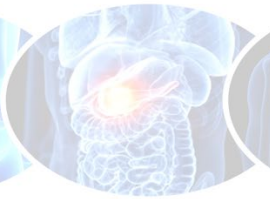
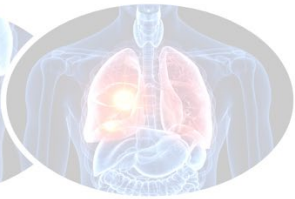
Rectal cancer	**Breast cancer**	Prostate cancer	Pancreatic cancer	Lung cancer
				
May 20th	**May 27th**	June 3rd	June 10rd	June 10rd
Keynote speaker: **Prof. C. Rödel**	Keynote speaker: **Prof. M. Brunt**	Keynote speaker: **Dr. N. van As**	Keynote speaker: **Prof. M. Hawkins**	Keynote speaker: **Prof. S. Senan**

QUESTIONS	ANSWERS
In FAST-Forward did the patients after mastectomy have reconstruction? Or it was only the chest wall irradiation?	264 had mastectomy, 26 of these had a mastectomy with immediate reconstruction.
Dear Prof, how did you select the dose regimens (5.7Gy/Fr, 5.4Gy/Fr, 5.2Gy/Fr) to compare with standard arms (50Gy/25Fr or 40Gy/15Fr)? What are the biological rationale?	When the FAST trial was being planned almost 20 years ago it was thought that the alpha-beta for long term normal tissue effects was going to be between 3 and 4. If 4 then the 30 Gy/5F was equivalent to 50/25 and if 3 the 28.5 Gy/5F was equivalent. In planning the FAST-Forward trial 10 years ago the alpha-beta was expected to be about 3 and the 27 Gy/5F would be equivalent but if it was as low as to then the 26 Gy would be equivalent.
Any concerns/data regarding heart doses/adverse events in ultra hypofractionation in left sided treatment? What are the constraints one should follow for heart/Lung doses?	With the current follow-up in FAST and FAST-FORWARD; there was no increase in cardiac and pulmonary toxicity in the 5-fraction arms
Good afternoon, question for Dr. Brunt: why it wasn't used simultaneous integrated boost for Fast Forward schedule ? It might improve waiting lists and accelerators workload? Tnks	SIB is for sure an interesting concept and probably the way forward. The sequential boost was chosen to achieve consistency with the START trials and standard practice. Several SIB trials are currently still recruiting. The dose for SIB would be unknown and would introduce an unacceptable variable. Also the planning for this trial was 10 years ago when this was not an option.
How many sessions can a patient miss without making a compensation in the 26/5 sessions schedule?	It's a good question. There is no standard answer and each situation has to be assessed as you would with any patient who has a break in treatment. Providing the treatment can be completed within two weeks, ideally with no more than one weekend in the schedule then I wouldn't make an adjustment.

What is your estimate for breast cancer alpha beta ratio?	The alpha-beta of 3.7 Gy for tumour control in FAST-Forward was very similar to the START 3-arm trials which gave a point estimate of 3.5 Gy. Point estimates assume no effect of time and this is a factor in biologically effective dose.
How did you generate the rationale to choose so little dose difference in Arm B and C of the Fast Forward trial? Did you expect measurable differences in toxicity or efficacy with only 1 Gy difference in total dose in advance?	Answered previously on alpha-beta. We did expect to see differences and this was proven to be the case.
Thanks for the great talk. Raquel Ciérvide, Radonc from Madrid, Spain. If you consider a simultaneous integrated boost for a future protocol, what dose would you consider?	Thank you. A simultaneous integrated boost is indeed a plan for a future trial. There is a lot of work that is going on with regard to this at the moment so I wouldn't want any figure to be taken out of context but it is likely to be quite close to 30 Gy in five fractions.
What OAR constraints do you use for 5 Fx?	As described in the study protocol which is available on open access.
Is there any range of breast volume (cc) with worst cosmetic outcome (photographic evaluation)?	There is evidence that patients with large breast volumes have an increased risk for radiation induced breast toxicity. There is no evidence to suggest that hypofractionation is a factor.
How do you do boost in your practice in the 5Fx setting? 3 x 2,67cGy? Do you consider single fraction boost?	I restrict the use of a boost to patients who have the most benefit and then use 13.35 Gy in 5 fractions.
In pN1 was the Axilla treated hypofrx or not at all	In the main trial the axilla was not irradiated. In the sub study for nodal radiotherapy the comparison is 40/15 against 26/5.
When you say you "offer" 5-fraction treatments to all patients, does that mean you explain to all patients that data is perhaps still a bit preliminary, and offer as well the 15-fraction option, or do you simply discuss 5 fractions as standard and not other options?	Yes, I would recommend to all patients with whole breast irradiation but currently not for nodal irradiation. Not only is the data published but also we have the support of the consensus meeting in the UK. I don't consider the data

	preliminary but I do think it is very important we will have the long-term results of 10 years.
Is it mandatory to have 3D Conformal or VMAT technique if we want to start offering 26Gy in 5 fractions?	Intensity modulated techniques are todays standard and are recommended irrespective of fractionation to achieve a homogeneous dose distribution
In how many patients was it difficult to achieve the OAR dose constraints and needed to be excluded from the trial	Only in the minority were the dose constraints difficult to meet. As centres became more experienced it became less likely they would meet a problem that they couldn't tackle. Some cases are always difficult and centres found that the quality assurance team would work closely with them. The advice was to make contact if the case was taking more than twice as long to plan. Very few if any were excluded from the trial.
In BCS + RNI setting, do you offer moderate hypofractionation to all patients	Yes
Can we offer moderate hypofractionation in reirradiation scenarios	A re-irradiation scenario has to be taken on an individual basis. The trials were not set up to look at this because all patients were radiotherapy-naïve. I would comment that 40/15 is more gentle on normal tissue than 50/25 and you would need to consider this in your calculations.
What is the time gap between CTRT and surgery	It depends. For example, in the Bondiau study (SBRT+ chemotherapy), surgery was performed 4-8 weeks after chemotherapy. In the Roth retrospective study, a time interval >2 months to surgery increased the probability of pCR.
Interesting results but in times of increasing neoadjuvant chemotherapy no gynecologist will allow me to do neoadjuvant radiotherapy	True. For example, with 70% pCR rates obtained after neoadjuvant chemo+ double immunotherapy for HER-2 + BC, the role of preoperative RTCT to increase pCR is minimal. However, in the context of a clinical trial,

	preoperative RT/RTCT might provide opportunities for other endpoints (toxicity after reconstruction) or pCR increase in other subtypes (ex TNBC, Luminal BC).
Is there a possibility of giving radiotherapy alone as the treatment of patients with early breast cancer in the future? (With no surgery)	This needs to be explored in the context of a clinical trial, but it might represent a true opportunity for less invasive treatment if the limitations of imaging in detecting pCR are overcome.
What about a "total neoadjuvant treatment" with intensified preoperative radiochemotherapy as in the paradigm of rectal cancer?	This could be an interesting concept especially for locally advanced BC, where endpoints such as pCR and breast conservation can be explored.
Do the 5 fractions have to be administered on consecutive days? Is an interruption over the weekend allowed?	It is not mandatory to deliver 5 fraction radiotherapy within one working week, a weekend in between is allowable.
Isn't it the systemic risk of progression that we are afraid of in high risk patients?	Yes, this is the case but also locoregional recurrence. The concern about recurrence of high risk patients is related to the disease and not to the use of 5-fraction hypo fractionation.
On what decision parameter did you select the boost dose of 10 vs. 16 Gy? Why normofractionated?	There are not hard decision criteria for or against one boost regimen. I personally favoured the 8-fraction regimen for the majority of patients because of the previous trial data. The debate over 10 years ago before we started FAST-Forward was whether or not we should use hypofractionated boost. There were arguments of course for using a hypofractionated boost but in the end we used normal fractionated boost so this was not a variable. We realise this created a situation where some patients could have three more fractions in the boost regimen than the main fractionation. Patient representatives on the trial were happy with this and this was not an issue that we encountered from patients offered entry to the trial.

Prof. Dr. M. Brunt

Prof Dr. P. Tsoutsou

Prof. Dr. M. Guckenberger