Dose response relationship of oligometastatic tumors treated with stereotactic body radiation therapy

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PURPOSE / OBJECTIVE

Oligometastatic tumors with limited number of lesions are known to be curable with ablative therapies. Stereotactic body radiation therapy (SBRT) is increasingly used as a curative strategy of various oligometastases. In this work, the dose response relationships of oligometastases treated with various SBRT fractionation schedules were evaluated, compared to the well-established early stage Lung SBRT dose response relationship.

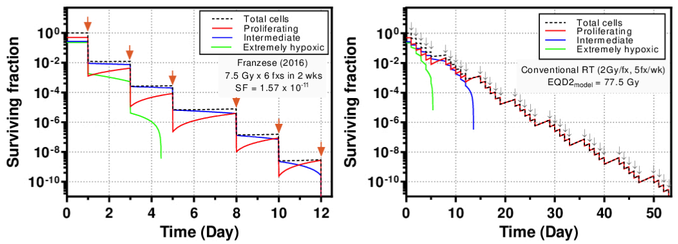
METHOD

Oligometastatic SBRT outcome data

- A thorough literature search was performed in PubMed databases
- With the query "(oligometastasis or oligometastases or oligometastatic) & (stereotactic or hypofractionated or hypofraction or "single fraction") & (outcome or outcomes) & ("local control")"
- Resulting 186 studies were reviewed
- Studies with more than 50 patients that report local control rate and enough information for model simulation were included

Estimation of model-derived equivalent dose 2Gy/fx ($EQD2_{model}$)

- In order to compare the treatment efficacy of various fractionations, cell kill effect was normalized through model simulation in conventional fractionation schedule, in terms of the model equivalent dose in 2Gy/fx ($EQD2_{model}$)
- Two-step simulation was performed: after cell survival fraction was estimated for a non-standard regime, another simulation was carried out for the conventional fractionation (2Gy/fx, 5fx/wk) until the same level of survival fraction is achieved



$EQD2_{model}$ estimation through the two-step simulation: after cell survival fraction is estimated for a given SBRT schedule (left); a conventional photon 2 Gy/weekday regime was simulated until the same level of survival fraction was achieved, resulting in an $EQD2_{model}$ (right)

Dose response relationship

- Dose response of each cohort was compared with the previously found dose response curve of early stage lung SBRT (Jeong et al., CCR 2017)
- Looking for potential risk factors that can explain the outcom result

RESULTS

Included studies

- 21 relevant studies were identified with enough information for model simulation and analysis
- 1643 patients and 2235 lesions with various oligometastatic sites and primary origins (table below)

Dose response relationship of oligometastatic tumors

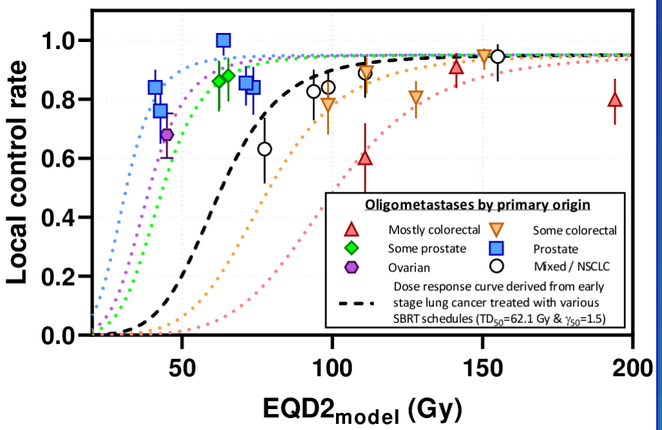
- For each cohort, population-weighted $EQD2_{model}$ value was found through simulation (table below)
- Compared to the early stage lung SBRT dose response curve (TD_{50}=62.1Gy, γ_{50}=1.5)
- Dose responses of the oligometastases broadly dispersed

Primary origin as a risk factor

- When grouped by the primary origin, a district dose response relationship was found for each group
- Cohorts with mixed origins or NSCLC generally agree with the previous dose response of lung SBRT
- Cohorts with the colorectal cancer origin seem to be more resistant (require about 60% extra dose in $EQD2_{model}$)
- Oligometastases with prostate or ovarian origin were evaluated to be more sensitive with lower TD_{50} values (30.9 and 38.5 Gy, respectively)

Oligometastatic SBRT outcome data included in the study (21 cohorts with 1643 patients and 2235 lesions). Primary origin of each cohort was categorized into 6 groups as highlighted in different colors matching with the dose response plot.

Reference	Total # patients	Total # lesions	Oligometastatic site(s)	Primary origin(s)	Population-weighted $EQD2_{model}$ (Gy)	Local control rate	Follow up time
Oh 2012	57	67	Lung	Mixed	155.1	0.95	2-year
Navarria 2014	76	118	Lung	Some colorectal	111.3	0.89	2-year
Owen 2014	74	85	Bone (non-spine)	Some prostate	62.4	0.86	2-year
Decaestecker 2014	50	70	Mixed (lymph node, bone)	Prostate	63.7	1.00	2-year
Comito 2014	82	112	Mixed (lung & liver)	Colorectal	194.1	0.80	2-year
Aitken 2015	73	87	Mixed	Some prostate	65.4	0.88	2-year
De Rose 2016	60	90	Lung	NSCLC	110.9	0.89	2-year
Goodman 2016	81	106	Liver	Mostly colorectal	141.3	0.91	2-year
Franzese 2016	71	79	Lymph node	Mixed	77.5	0.63	2-year
Agolli 2016	44	69	Lung	Colorectal	110.9	0.60	2-year
Jereczek-Fossa 2017	94	124	Lymph node	Prostate	41.1	0.84	2-year
Chang 2017	60	72	Spine	Some prostate	62.2	0.86	2-year
Gandhidasan 2018	132	186	Mixed (lung, bone...)	Mixed	98.7	0.84	2-year
Dohopolski 2018	105	185	Lung	Some colorectal	150.5	0.94	2-year
Fanetti 2018	55	77	Bone	Prostate	42.8	0.76	2-year
Lazzari 2018	82	156	Mixed (abdo/pelv, thorax)	Ovarian	44.9	0.68	2-year
Loi 2018	91	91	Lymph node	Some colorectal	98.6	0.78	2-year
Franzese 2018	64	90	Mixed	Prostate	73.7	0.84	18-month
Osti 2018	129	166	Lung	Some colorectal	127.8	0.80	3-year
Ouyang 2019	71	86	Lung	NSCLC	93.8	0.83	2-year
Franzese 2019	92	119	Mixed	Prostate	71.2	0.86	3-year



Dose response relationship for oligometastatic tumors, overlaid with the dose response curve of early stage lung cancer for various fractionation schedules (black dash). Dose responses vary by primary origins and a distinct dose response curve was derived for each group of primary origin (dotted color lines). Cohorts from colorectal origin are more resistant, while prostate and ovarian origins are more sensitive.

SUMMARY

In this work, dose response of various oligometastatic tumors to SBRT was evaluated. Primary origin seems to affect the dose response relationship. Oligometastases originated from colorectal cancer are more resistant, while prostate or ovarian origin are more sensitive. Further investigation with more data is needed to validate these findings.

REFERENCES / ACKNOWLEDGEMENT

Jeong, et al. (2013). PMB, 58(14), 4897.
Jeong, et al. (2017). CCR, 23(18), 5469-5479.

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