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Radiation
Oncology

Sparing the heart reduces early function loss of the rat lung most for small irradiated volumes:

Potential benefit for proton therapy compared to photon therapy

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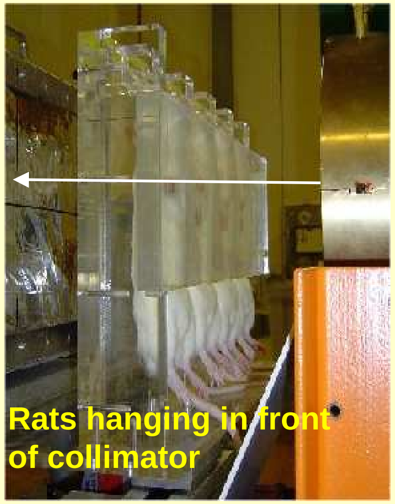
PURPOSE

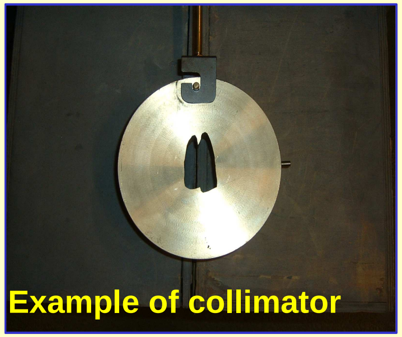
In previous work we showed that co-irradiation of the heart reduces the tolerance dose for radiation-induced pneumonitis in the lung of the rat [1].

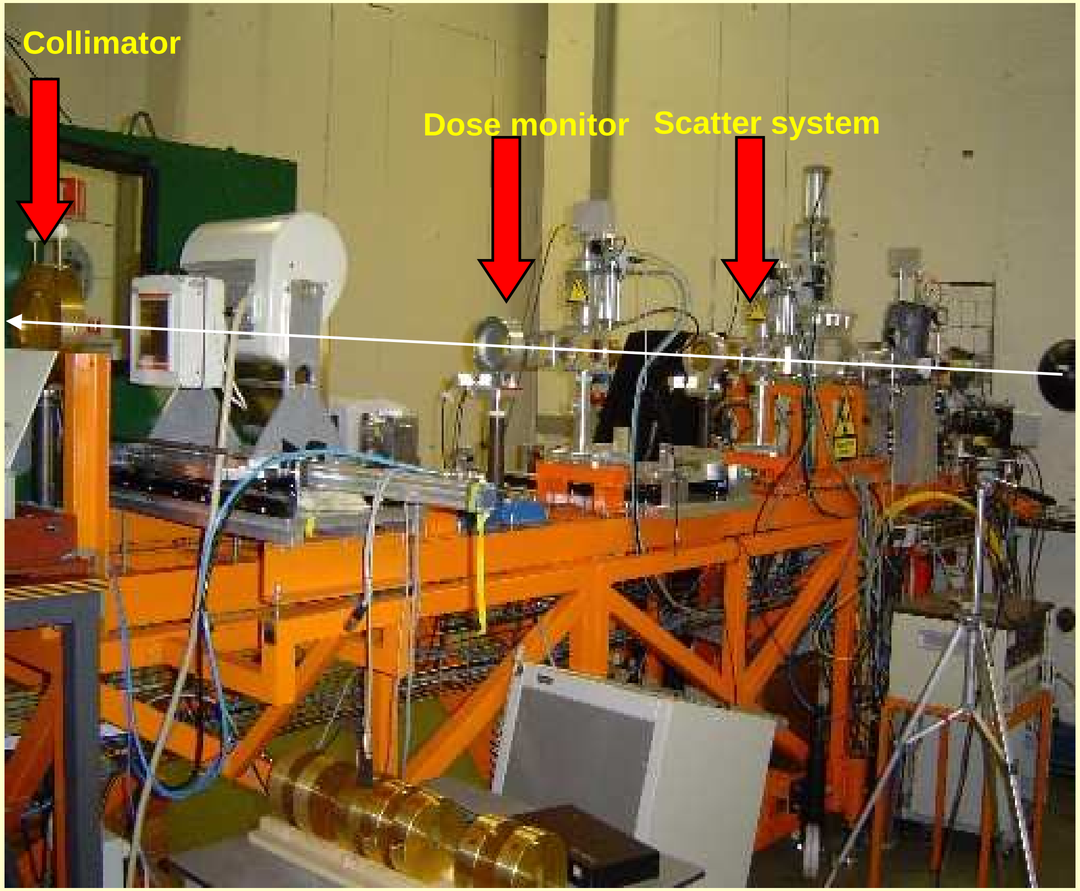
In the present study we investigated the dependency of this effect on the irradiated lung-volume

1 Peter van Luijk, et al.
Radiation Damage to the Heart Enhances Early Radiation-Induced Lung Function Loss.
Cancer Res 2005; 65(15): 6509-11

MATERIALS & METHODS







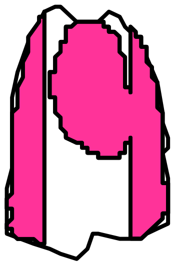
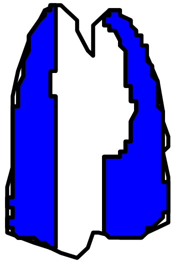
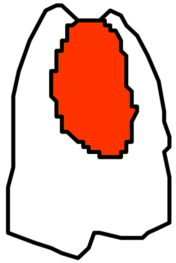
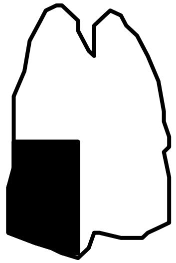
Set-up for the irradiation of the rats at the Kernfysisch Versneller Institute in Groningen

Lungs of Wistar rats were irradiated in anterior-posterior direction with 150 MeV protons, using the shoot-through technique.

Groups of 5-7 animals received a single dose ranging from 16 to 36 Gy

MATERIALS & METHODS

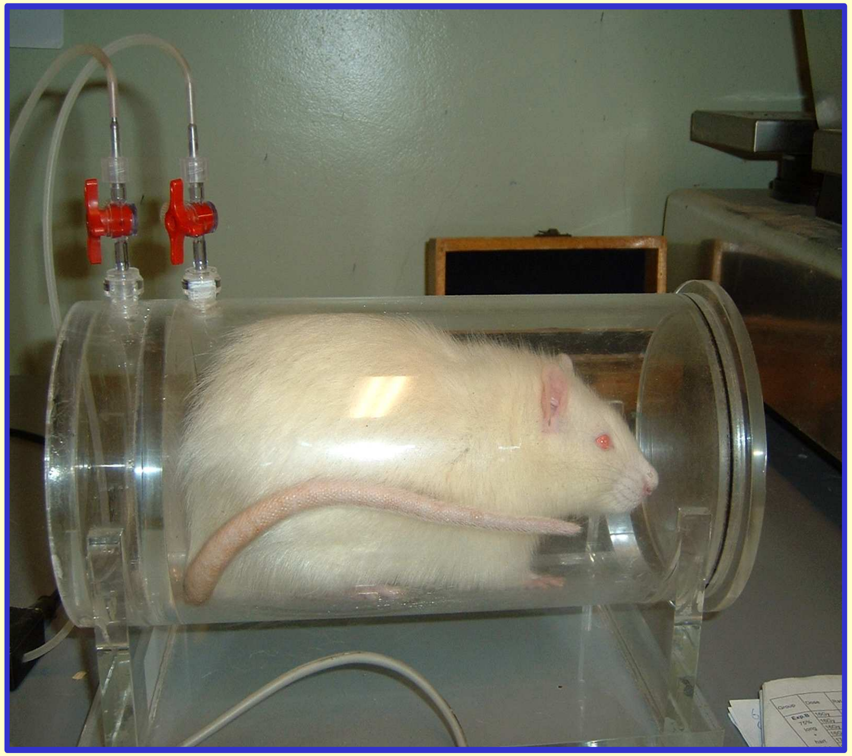
Radiation portals used and dose given

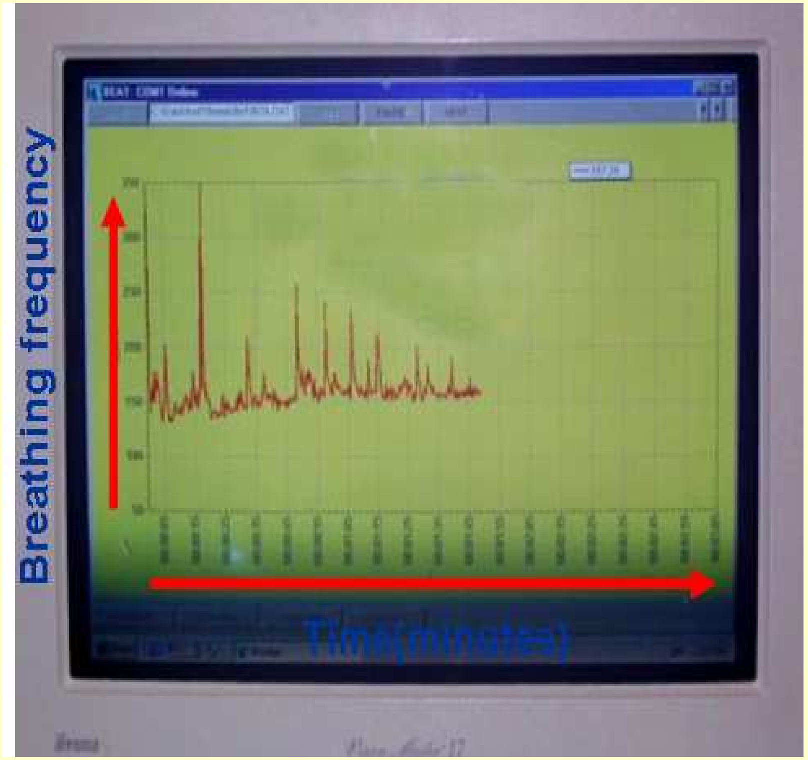
Radiation port				
Lung (% volume)	50	50	25	25
Heart (% volume)	100	0	100	0
Dose (Gy)	16-21	16-21	19-23	28-36

Four different ports for irradiation of 50% and 25% lung-volumes, both including and excluding the heart.

MATERIALS & METHODS

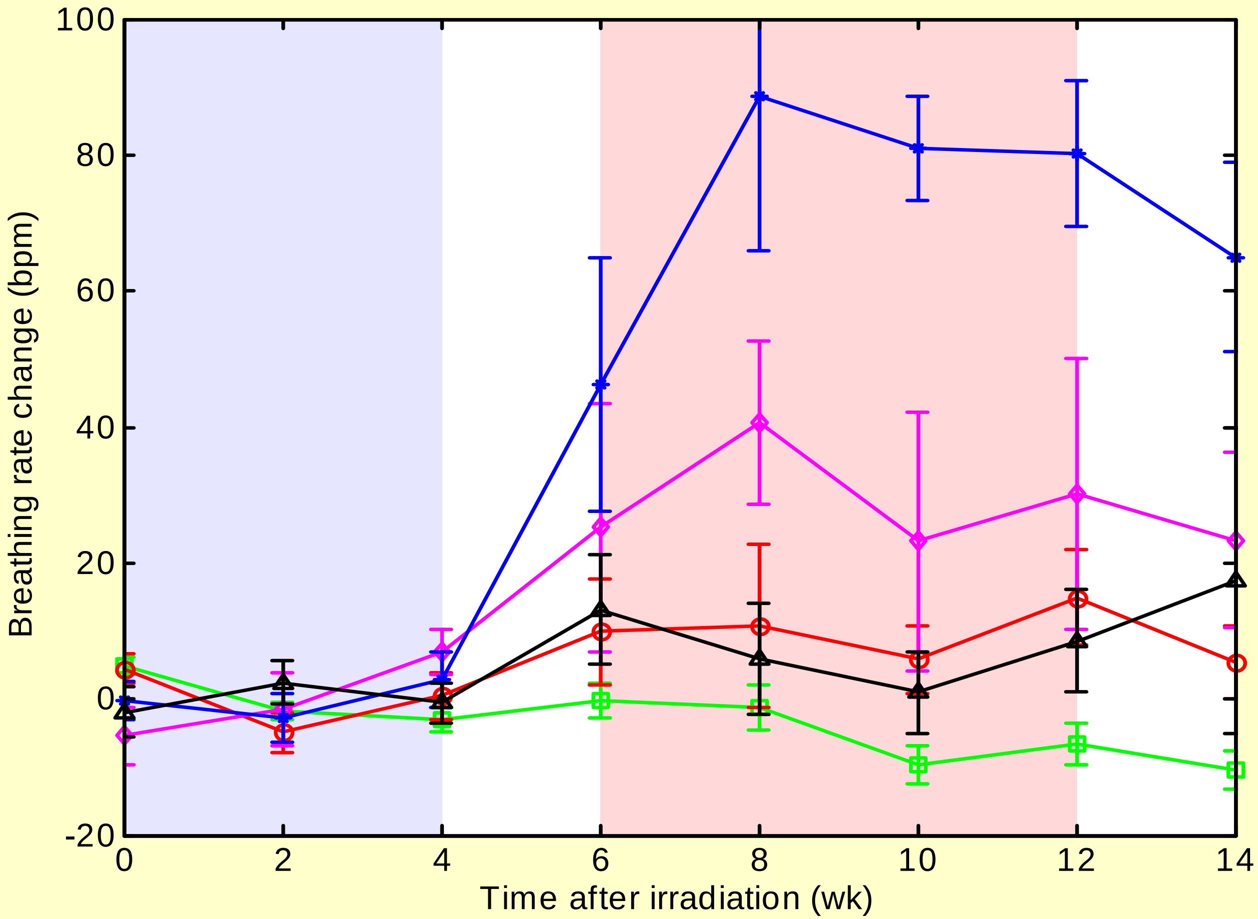
Set-up for the measurement of the breathing rate (BR)





Breathing rate (BR) measurements were performed bi-weekly

Obtaining binary data



In the weeks 6-12 after irradiation there is an increase in BR

MATERIALS & METHODS

The increase of the mean BR in this period, relative to the mean BR in week 0-4 after irradiation for the same rat, was used as an indicator of the functional status of the lung.

Induced function loss was determined using a threshold on the increase in BR.

An increase of BR above this threshold was defined as a symptomatic loss of lung function (SLLF).

MATERIALS & METHODS

For each dose group the fraction of animals with SLLF was determined, which equals the NTCP.

For each dose-distribution, probit curves were fitted to these NTCP data and the dose for which 50% of the animals responded was derived (ED_{50}) as well as the steepness (m) of the probit curve.

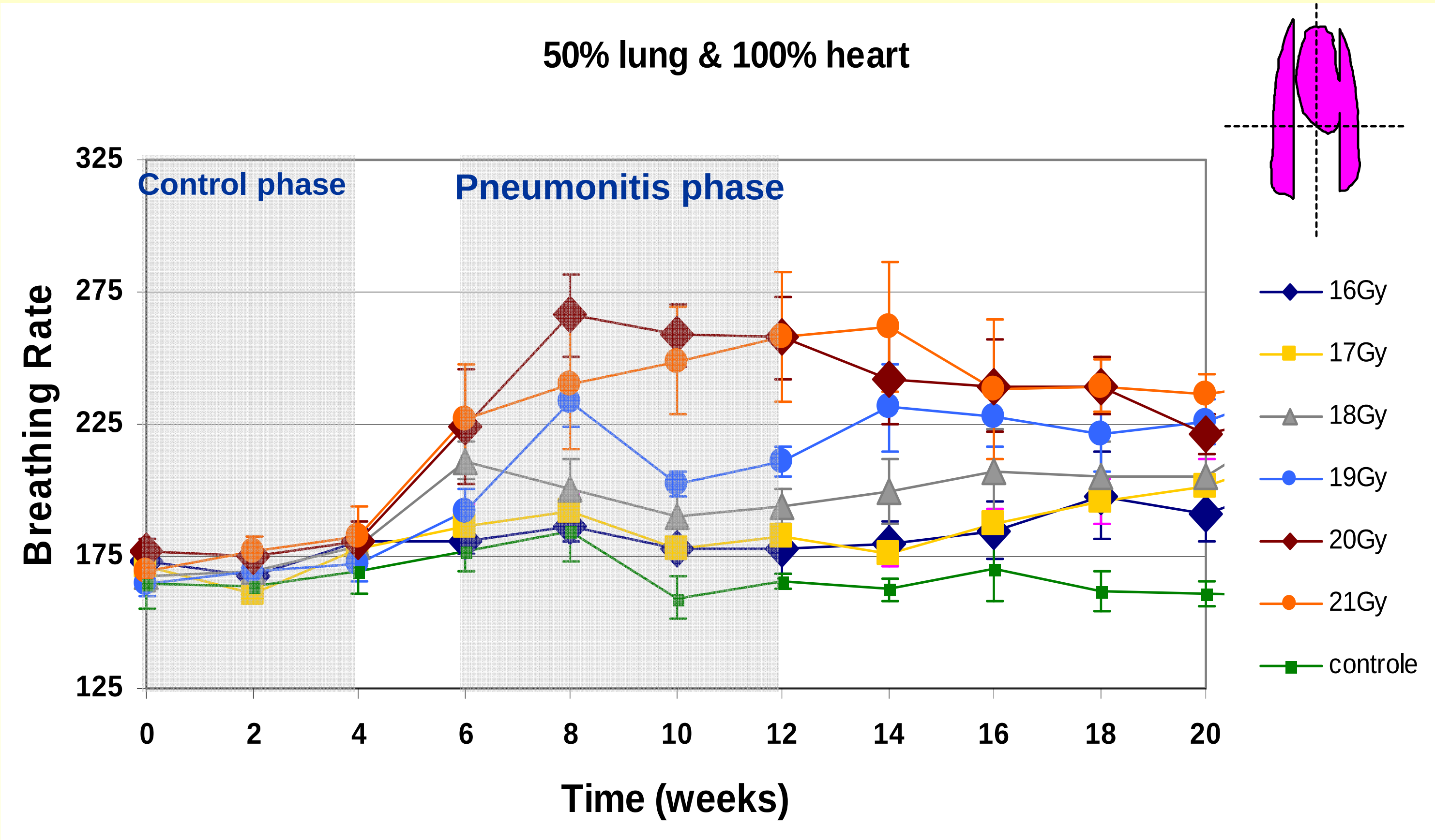
The maximum likelyhood (LL) procedure was used to fit the probit model to the data.
The confidence intervals for ED_{50} and m where derived directly from the LL- landscape.
The iso-LL contour that is at the value: $LL_{max} – (0.5*2^2)$, indicates 2 SD

RESULTS

The threshold calculated from the control animals was 19 beats per minute.

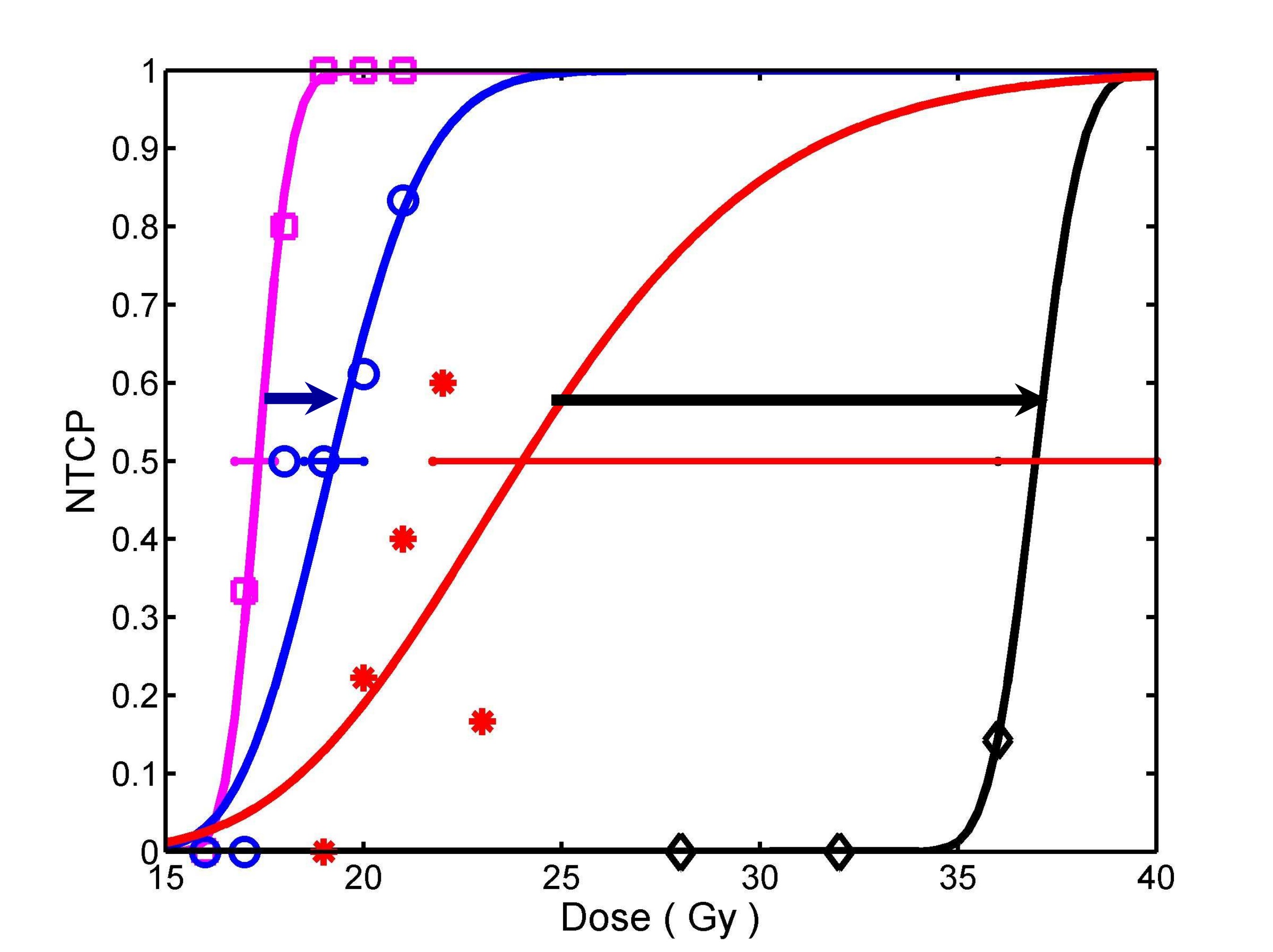
All other animals showed during the period from 6 to 12 weeks after irradiation a significant increase in BF for an increasing dose.

RESULTS



Breathing Rate as a function of time after irradiation.
Radiation port : 50 % lung, 100% heart.
Dose range: 16 to 21 Gy.

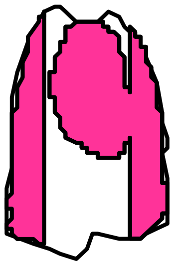
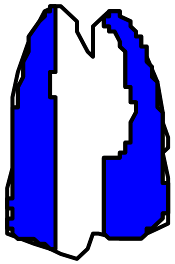
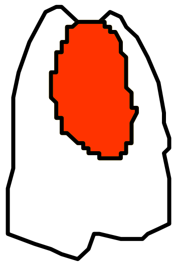
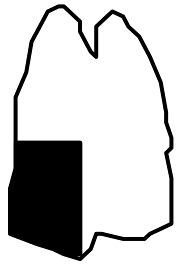
RESULTS



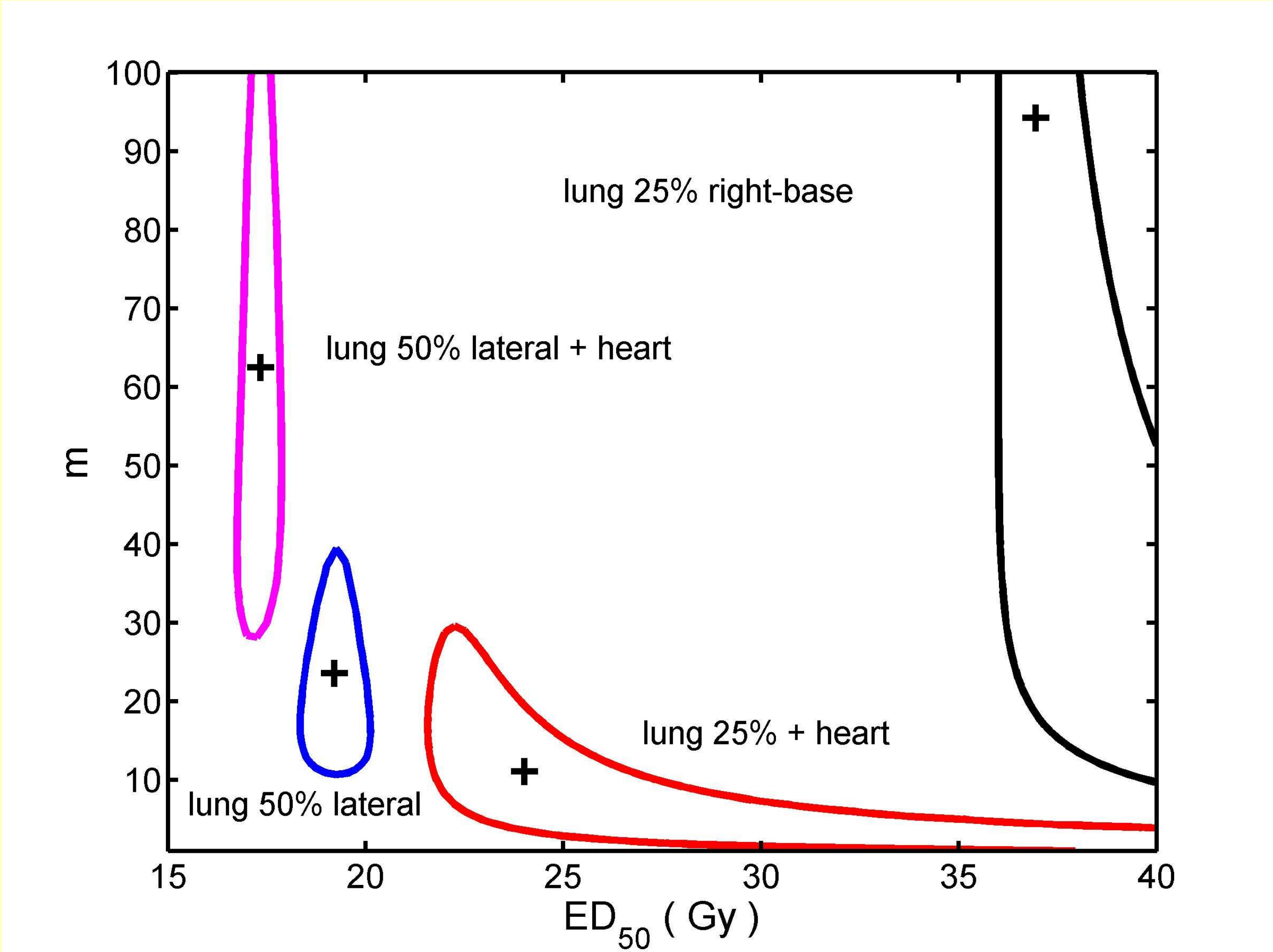
NTCP points for the four irradiatiation ports and corresponding probit curves fitted to this NTCP data

RESULTS

Radiation portals used, dose given and resulting values for ED_{50} and slope parameter m.

Radiation port				
Lung (% volume)	50	50	25	25
Heart (% volume)	100	0	100	0
Dose (Gy)	16-21	16-21	19-23	28-36
ED_{50} (Gy)	17.3	19.2	24.0	36.9
slope m (Gy^{-1})	62	24	11	94

RESULTS



Cross sections of the LL-landscape showing the 95% confidence regions of the fitted ED_{50} parameter and slope parameter m.

SUMMARY

Irradiation of a 50% volume of lateral lung tissue combined with 100% heart resulted in an ED_{50} of 17.3 Gy.

If the heart was spared, the ED_{50} becomes 19.2 Gy, an **increase** in ED_{50} **of 1.9 Gy**.

Irradiation of a 25% volume of right base of the lung, combined with 100% heart, resulted in an ED_{50} of 24.0 Gy.

When the heart was spared the ED_{50} becomes 36.9 Gy an **increase** in ED_{50} **of 13 Gy.**

The differences between the four set-ups were significant.

DISCUSSION

Proton and photon irradiation techniques are continuously under development to further improve the dose distribution e.g. in thoracic regions in order to escalate the dose to the tumor and/or to reduce the dose to organs and tissues at risk.

The volume of the co-irradiated lung tissue is smaller in proton irradiations than in photon irradiations.

Therefore, our findings suggest that the benefit of sparing the heart might be substantially greater in proton therapy, which may result in enhanced opportunities for dose escalation compared to photon based techniques.

Sparing the heart might result in a significant reduction of early radiation induced symptomatic loss of lung function.

CONCLUSIONS

The effect of dose to the heart on the tolerance dose for early symptomatic loss of lung function depends strongly on the irradiated lung volume

For small irradiated lung volumes this effect is significantly larger than on larger irradiated volumes

This might have a clinical relevance especially for dose escalations performed at small lung volumes like for instance in proton therapy

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