

cases were 89%, 89%, and 65%, 43%, respectively ($p=0.055$). Patterns of initial relapse were, local in 11 cases, pleural in 5, nodal in 8, and distant in 13. There were 7 Grade 3 pulmonary toxicities (6%), but there were no severe adverse effects concerning serial organs.

Conclusions: Three-DNCCRT for stage I non-small cell lung cancer has been safe and effective for not only inoperable but also operable cases, and equally effective for peripheral and central tumors, and T1 and T2 tumors. Our treatment might be an alternative to SBRT especially central tumors and T2 tumors, which the results of SBRT have not been satisfactory.

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Dose painting by numbers for NSCLC: probabilistic evaluation of the impact of uncertainties on target dose coverage

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Purpose/Objective: Locally advanced non-small cell lung cancers (NSCLC) are typically treated with 60 to 66 Gy in 2 Gy fractions. Local control for this treatment is poor, but it could potentially be improved by increasing dose to the more therapy resistant areas, e.g., based on the SUV uptake values on the pre-treatment FDG-PET scan. This is the dose painting by numbers (DPBN) approach, which intrinsically does not allow a conventional PTV margin. This study investigates the influence of random and systematic errors on target dose coverage with DPBN, in terms of difference between dose to 99% of GTV volume ($\Delta 99$) when geometric errors are considered. For example, $\Delta 99 = -10$ Gy means that, for 99% of the target volume, the dose delivered is decreased by no more than 10 Gy compared to the planned dose.

Materials and Methods: 9 DPBN plans of stage II/III NSCLC patients were considered; a minimum dose of 66 Gy at 2-Gy fractions was prescribed to the entire CTV with a boost dose to the high SUV areas within the primary GTV, using a non-uniform dose prescription linear with the underlying FDG PET SUV. The boost dose was escalated up to 130 Gy (in 33 fractions) or until the dose limiting constraint of an organ at risk was reached. Then, using Monte Carlo methods, a probabilistic evaluation of dose endpoints at 90% confidence was performed considering 8 different combinations of systematic (Σ) and random (σ) geometric uncertainties, taken as standard deviations identical in x, y and z axes: $(\Sigma, \sigma) = (5,2); (4,2); (3,2); (2,2); (3,4); (3,3); (2,3);$ and $(1,2)$.

Results: The impact of geometric errors on the ability to paint dose is important, and significant discrepancies of up to 38 Gy occur (Table 1).

	Σ [mm]	σ [mm]	$\Delta 99$ [Gy]		Σ [mm]	σ [mm]	$\Delta 99$ [Gy]		Σ [mm]	σ [mm]	$\Delta 99$ [Gy]
Patient 1	5	2	-4.49	Patient 4	5	2	-35.49	Patient 7	5	2	-23.05
	4	2	-3.78		4	2	-29.44		4	2	-18.95
	3	2	-2.97		3	2	-22.59		3	2	-13.8
	2	2	-1.67		2	2	-15.06		2	2	-8.43
	3	4	-2.98		3	4	-24.26		3	4	-14.59
	3	3	-2.95		3	3	-23.2		3	3	-14.05
Patient 2	2	3	-0.53	2	3	-22.6	2	3	-9.15		
	1	2	-0.22	1	2	-7.54	1	2	-3.57		
	5	2	-3.67	5	2	-13.36	5	2	-4.4		
	4	2	-2.51	4	2	-9.6	4	2	-3.49		
	3	2	-1.67	3	2	-6.06	3	2	-2.3		
	2	2	-0.99	2	2	-3.13	2	2	-1.12		
Patient 3	3	4	-1.78	3	4	-6.3	3	4	-1.91		
	3	3	-1.67	3	3	-6.11	3	3	-2.07		
	2	3	-0.99	2	3	-3.3	2	3	-1.43		
	1	2	-0.44	1	2	-1.25	1	2	-0.82		
	5	2	-37.83	5	2	-30.1	5	2	-16.34		
	4	2	-31.39	4	2	-24.94	4	2	-12.76		
Patient 4	3	2	-23.98	3	2	-18.7	3	2	-8.18		
	2	2	-15.66	2	2	-11.98	2	2	-3.4		
	3	4	-26.62	3	4	-18.84	3	4	-8.94		
	3	3	-24.98	3	3	-18.57	3	3	-8.46		
	2	3	-17.75	2	3	-11.84	2	3	-4.97		
	1	2	-7.88	1	2	-5.46	1	2	-1.39		

Table 1: Discrepancy between prescribed and evaluated dose at 90% confidence in 99% of the volume ($\Delta 99$) for the different combinations of systematic and random geometric uncertainties considered. The loss of dose can be rather high, up to almost 38 Gy (patient 5 with $(\Sigma, \sigma) = (5,2)$, at 99% of the volume).

The evaluation showed a clear dependence of $\Delta 99$ on systematic errors (Fig. 1); the influence of random errors was less pronounced. The effects of the uncertainties are shifted and smoothed dose peaks; indeed the largest differences between planned and delivered dose occur where the dose or its gradient are high.

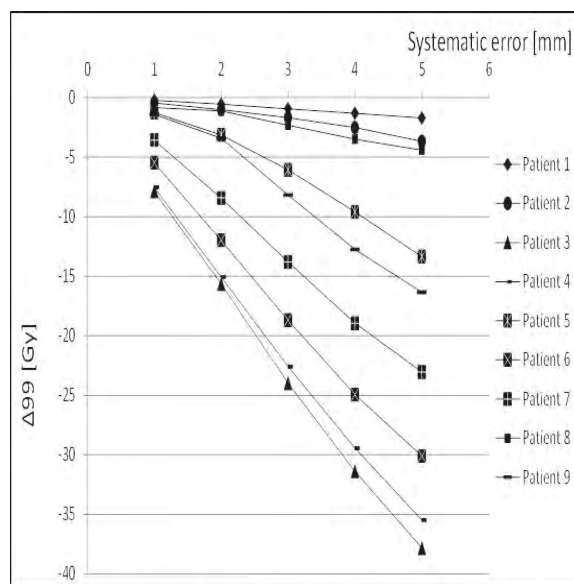


Fig 1: Loss of dose to 99% of the volume ($\Delta 99$) at 90% confidence as a function of systematic errors (Σ) for the different patients. The effect of random errors was much smaller.

Conclusions: A probabilistic evaluation of 9 DPBN plans showed that geometric uncertainties should be taken into account before approving the plans for treatment, otherwise significant hidden discrepancies between prescribed and delivered dose distributions will occur. The discrepancies become more acceptable when the systematic errors become small ($\Sigma < 2$ mm), which strongly suggests that DPBN should be paired with an accurate IGRT. Probabilistic optimization, taking uncertainties into account also at the planning stage, might intrinsically mitigate the reported issues.