SABR versus conventional fractionation regimens in NSCLC

The results of the CHISEL trial showing superiority of stereotactic ablative body radiation therapy (SABR) in stage I non-small cell lung cancer (NSCLC) will be welcomed by all radiation oncologists.[1]

The control group of this trial permitted two regimens—50 Gy in 20 fractions or 66 Gy in 33 fractions—and claimed to reflect real-life practice. However, when comparing biologically effective dose, the 50 Gy regimen is clearly suboptimal.[1] The repopulation corrected biologically effective dose is 72·4 Gy_{10} for the 66 Gy regimen and 62·5 Gy_{10} for 50 Gy (α/β 10 Gy, repopulation factor 0·4 Gy/day, and kick-off time 28 days).[2] Indeed, the preferred hypofractionation schedule in this setting is 55 Gy in 20 fractions, which has a biologically effective dose of 70·1 Gy_{10}.[3] This regimen was widely used in the UK and many other countries even at the time the CHISEL trial commenced recruitment.[3]

Indeed, nearly 30% (10/35) of patients in the control group were treated with 50 Gy and a post-hoc analysis of overall survival between the control group regimens revealed a non-significant (p=0·12) trend of inferior overall survival for the 50 Gy regimen with a hazard ratio (HR) of 0·49. Not reaching statistical significance is due to the small sample size. Although most patients in the control group received 66 Gy, the magnitude of the HR (0·53) raises doubt as to whether the superiority of SABR was mainly driven by the inferior overall survival of patients treated with 50 Gy. It is relevant that the SPACE trial, in which the control group received 70 Gy, did not show an improvement in overall survival with the use of SABR.[4]

As such, it is questionable whether the results of the CHISEL trial allows a safe inference of superiority (in terms of overall survival) of SABR over conventional fractionation regimens. Because small numbers did not deter the investigators from comparing overall survival between control group regimens, we suggest that the authors could do a subgroup analysis of overall survival by treatment group against the control group fractionation regimen. Although likely to be still underpowered, the comparison would allow the data to speak for itself, and such an analysis would shed light on the effect of fractionation regimen in the control group on the overall results.

Some oncologists might claim that SABR as standard of care in this setting is already a *fait accompli*. However, accurately confirming the treatment's superiority over conventional regimens will be of pivotal importance to those seeking robust evidence to change their practice.

We declare no competing interests.

*Nuradh Joseph, Ananya Choudhury
nuradh@gmail.com

Ministry of Health, Colombo 01000, Sri Lanka (NJ); Division of Cancer Sciences, Faculty of Biology, Medicine and Health, The University of Manchester, Manchester, UK (AC); and The Christie NHS Foundation Trust, Manchester, UK (AC)

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2 Fowler JF. 21 years of biologically effective dose. *Br J Radiol* 2010; **83:** 554–68.

3 Willams MV, James ND, Summers ET, et al. National survey of radiotherapy fractionation practice in 2003. *Clin Oncol* 2006; **18:** 3–14.

4 Nyman J, Hallqvist A, Lund JÅ, et al. SPACE—a randomized study of SBRT *vs* conventional fractionated radiotherapy in medically inoperable stage I NSCLC. *Radiother Oncol* 2016; **121:** 1–8.