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Curative radiotherapy for NSCLC: Practice changing and changing practice?

In the UK there are still 42,000 cases of lung cancer diagnosed each year and as the past decade has seen several practice changing developments in the management of this disease, history has always taught us that patients have their best chance of a good treatment outcome if their cancer is diagnosed at an early stage. In addition to smoking cessation, it is the early diagnosis and treatment of lung cancer that is the most effective way to reduce lung cancer mortality at this point in time [1].

Over the past 20 years the practice of lung oncology has undergone radical change with the establishment of multi-disciplinary team working to ensure guideline-recommended staging procedures and treatments. In the UK a prospective national audit program has shown that in addition to the improvements documented in all modalities of treatment, there has been significant improvement in survival across all stages of the disease. With technical advances in radiotherapy planning and delivery, the question arises as to when is the appropriate time and what level of evidence is required to change practice? It is with this background that two of the articles, both using linked datasets to supplement data collected through the National Lung Cancer Audit in 2015 – 16, concentrate on curative intent radiotherapy approaches in current day to day practice across the UK [2, 3].

In the first article, Phillips et al [2] study the treatment modality and outcomes for patients presenting with Stage 1 NSCLC, showing just over 70% of patients were treated with curative intent with around 20% receiving radical radiotherapy. The focus of the paper is on the planning and delivery of the radiotherapy which has benefited from several major developments including 4D-CT scanning and IMRT which have transformed treatment planning and online imaging with cone beam CT has significantly improved the accuracy of delivery. These improvements have permitted the development of Stereotactic Ablative Radiotherapy (SABR) techniques and dose fractionation schedules. The authors have raised concerns that around one quarter of patients with stage I NSCLC receive no curative treatment and another third were treated with more conventional fractionation rather than SABR. Both these proportions are high in comparison to other developed counties [4, 5] and are likely to be related to continued limited availability of SABR across the UK.

The use of SABR for early stage lung cancer was first described in 1994, and the Dutch were early adopters in Europe in 2003. Based on comparative effectiveness studies in the Dutch population,

together with single-arm prospective studies, ESMO recommended SABR as a standard of care treatment in 2013 [6]. In contrast, the UK has been very cautious in its introduction of lung SABR, with concerns expressed about potential toxicity of SABR, and in part the higher level of evidence available for the CHART approach rather than SABR [7]. However, that higher level of evidence for SABR is now available, with a recent randomised controlled trial showing an improvement in both local control and survival with SABR compared with more conventionally fractionated radiotherapy [8]. It is important that the UK now catches up to ensure patient access to SABR across the UK to achieve the survival gains observed with this technique.

The paper by Phillips et al reports that patients undergoing SABR in England have increased from 64% in 2015, to 73% in 2016. Importantly, the 2018 updated UK SABR Consortium Audit [9] documents an increase in SABR provision with the number of centres commissioned to deliver SABR rising from 12 in 2012 to 38. However, the survey also demonstrated that SABR is not currently offered in around 40% of UK radiotherapy centres, a finding that highlights that the concerns raised by Phillips et al from the 2015-16 data are still present. The results relating to travel time suggest that improvements in SABR provision and commissioning across the UK are urgently needed to ensure that medically inoperable and high risk surgical patients are offered SABR over more conventional radiotherapy or no treatment, both associated with worse outcomes. It would be of interest to understand whether there is disparity in accessing SABR amongst vulnerable groups of patients such as the elderly and poor socio-economic groups.

In the second article, Harden et al [3] assess the treatment modality and outcomes for patients presenting with Stage III NSCLC over the same time period and reveal that only 30% of patients received a radical intent treatment (surgery or radical radiotherapy) and only 18% received multimodality treatment including chemotherapy and either surgery or radical radiotherapy. Sequential chemoradiotherapy was delivered almost twice as often as concurrent and a staggering one third of patients received active palliative treatment and over a third received best support care alone.

For inoperable disease multi-modality treatment with concurrent chemoradiotherapy is the standard of care in good performance status patients. Concurrent chemoradiotherapy is associated with improved outcomes compared to sequential chemoradiotherapy or radiotherapy alone [10, 11]. However, the modest overall survival gains at 3 and 5 years reported by these meta-analyses balanced against the increased toxicities has meant the sequential approach has remained popular

in the UK with the widespread use of CHART and other accelerated radiotherapy schedules potentially offering the improvement in local control reported for the concurrent approach.

It is striking that the more recent studies that have used PET staging to confirm stage III disease (e.g. RTOG 0617 [12], PROCLAIM [13]) document much improved median and 5 year survival compared to those reported in the meta-analyses. In the absence of similar reported outcomes for the sequentially treated patients it is these data together with the recently reported gain in survival with Durvalumab after concurrent chemo-radiotherapy [14] that should be swinging us towards the use of the concurrent approach, at least for those patients who meet the trial eligibility criteria.

The article discusses that the rates of optimal treatment are lower than the rates reported in other international population-based studies and the associated poor clinical outcome data reflects this. The question arises as to why there are such low rates of patients receiving radical treatment in the UK? The UK lung cancer community needs to address the reasons behind this as a matter of urgency. Of particular concern is the regional variation of between 8% and 80% in curative treatment being received by patients with stage IIIA NSCLC. Outdated practices and nihilist attitudes in multi-disciplinary teams need to change and access to optimal radiotherapy with i.v. contrast, motion management and IMRT planning in addition to cone-beam CT image-guided delivery need to be ensured.

The most promising leap forward in treatment and outcomes for inoperable stage III disease for many years was published last year, demonstrating a significant additional survival advantage with the addition of adjuvant Durvalumab for 1 year following concurrent chemoradiotherapy [14]. With the recent NICE approval for this treatment in patients whose tumours express PDL1, the UK need to catch up and ensure best practice for appropriate patients and avoid falling further behind other countries. Commissioning of advanced radiotherapy techniques across the regions and reimbursement of planning to assess ‘encompassibility’ of treatment volumes in a radical radiotherapy treatment plan also need to be provided.

It is important to note the completeness of the dataset reported on in these two important articles. With such a high proportion of patients being captured, a realistic denominator is reflected in the population figures. With the methods in place to continue assessing the data annually going forward, the team involved in the national lung cancer audit over the next few years stand to contribute greatly to ensuring practice changing evidence is implemented widely for the benefit of our patients.

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