Radiation therapy (RT) is employed in all stages of lung cancer. In this article, I will highlight some areas where improvement is needed. We at the National Cancer Institute (NCI) welcome proposals addressing those needs.

**Early stage non-small cell lung cancer (NSCLC)**

Many such cancers can be cured by RT. A prospective randomized trial showed that treatment with three fractions was just as effective as 35 fractions with regard to 3-year PFS and, furthermore, was less toxic and much more convenient for the patients (1). However, about 30% of those patients suffered local-regional and/or distant relapses. Imaging and/or blood-based biomarkers are needed for identifying the subsets of patients destined to suffer relapses and for testing novel interventions that may prevent relapses, such as immune modulation or targeted radionuclides (2).

Subsequently, another prospective randomized trial showed that a single fraction of SRT was safe and, furthermore, was just as effective as multi-fraction SRT (3). Very few local relapses were observed in that trial but imaging and/or blood-based biomarkers may be helpful for developing and testing interventions that can predict and/or prevent relapses elsewhere.

**Locally advanced NSCLC**

Most patients are treated by RT with or without systemic therapy. Only a minority survive long-term while most succumb to local and/or distant failure. Administering a higher radiation dose was, surprisingly, associated with worse survival in a prospective randomized trial (4). Adaptive therapy guided by FDG-PET as a biomarker is being studied at present but it is not yet known if it improves outcomes.

It is becoming apparent that there are numerous subtypes of NSCLC (5). Different subtypes may have different vulnerabilities to different drugs or to different types of radiation (6). Imaging and/or blood-based biomarkers will likely prove very important in developing and testing the most appropriate therapy for each subtype.

**Limited disease-small cell lung cancer (LD-SCLC)**

Most patients are treated by concomitant CRT plus PCI but a recent prospective randomized trial found that about two-thirds of the patients suffered relapses in the chest or elsewhere and only about one-third survived for 5 years (7). Imaging and/or blood-based biomarkers will be helpful for identifying the subsets of patients destined to suffer relapses and for testing novel interventions such as immune modulation or targeted radionuclides that may prevent relapses.

Some patients exhibit neurocognitive deficits even before PCI but there is very little evidence that PCI in general worsens the neurocognitive function. If there indeed exists a subset of patients more susceptible to neurocognitive decline after PCI, imaging and blood-based biomarkers may be helpful in identifying that subset.

**Extensive disease-SCLC (ED-SCLC)**

Most patients are treated by chemotherapy and usually
die within two years. For those patients that responded to chemotherapy the addition of PCI led to a slight prolongation of survival in a prospective randomized trial (8), imaging and/or blood-based biomarkers may be helpful for developing and testing novel interventions that can increase the remission rates and improve the dismal outcomes.

There are growing opportunities from NCI to support research relating to imaging and biomarkers for precision medicine in lung cancer. Overall NIH study sections can be located on https://public.csr.nih.gov/studysections/standing/pages/default.aspx. Current available resources include (not limited) the following:

- Biomarker: https://public.csr.nih.gov/StudySections/IntegratedReviewGroups/OTCIRG/CBSS/Pages/default.aspx;

As these resources are constantly updating, the readers are also advised to contact individual officials like myself that can be located at NCI website https://rrp.cancer.gov/aboutRRP/bios/vikram_bhadrasain.htm.

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Footnote

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