

The Path to Lung Cancer Control: Combine Surgery with Stereotactic Radiotherapy

An article on the role of stereotactic ablative radiotherapy (SABR), also known as stereotactic body radiation therapy (SBRT), in the treatment of resectable stage I non-small cell lung cancer (NSCLC) published in the *Lancet* in 2015 has stirred up new debates (DOI: [http://dx.doi.org/10.1016/S1470-2045\(15\)70168-3](http://dx.doi.org/10.1016/S1470-2045(15)70168-3)). This article compared the efficacies of SABR and lobectomy for resectable stage I NSCLC based on the findings of two randomized controlled trials (RCTs) (i.e. the STARS study, initiated by the MD. Anderson Cancer Center; and the ROSEL study, from the Netherlands). Totally 58 patients were enrolled in these two studies. The 3-year overall survival (OS) rates were 79% and 95%, respectively, in the lobectomy group and SABR group, and the 3-year recurrence-free survival (DFS) rates were 80% and 86%, respectively. The SABR group had significantly lower incidences of serious toxic reactions than the lobectomy group. The study concluded that SABR could be well tolerated in resectable stage I NSCLC patients and thus could be an important option for these patients. However, this study has been widely criticized on the grounds that: (I) the sample size was too small; (II) no pathological results were obtained from some patients; (III) the pathology and lymph node staging were not definite in some patients; (IV) the case-fatality rate was unproportionally high in the lobectomy group; and (V) the follow-up duration was too short. In fact, these limitations had been frankly described in the article.

While there are many controversies, one of its conclusions is particularly valuable: SABR is safe and effective in treating resectable stage I NSCLC. Obviously, this was not a perfect study—perhaps there is no perfect research in clinical settings. Despite the presence of these limitations, generations of clinical researchers have constantly launched and updated clinical trials in their search for truth. In my opinion, this study not only presented a new treatment option other than surgery for selected patients with phase I lung cancer but also, and maybe more importantly, provided a key ethical basis for similar clinical research in future—both patients and researchers will be mentally more willing to accept this new technique. It can be expected that more similar multi-center RCTs with larger sample sizes will be available in the coming years and more widely accepted and recognized evidence-based conclusions will be reached. Naturally, we often do not know what we do not know and the truths are often behind paradoxes; a relatively firm conclusion can not be drawn without repeated investigations and discussions. Currently, clinicians from the United States, the United Kingdom, and China are carrying out larger phase III RCTs to compare the efficacies of SABR and surgery. The results might be promising.

As a radiation oncologist, I am particularly interested in these two studies—STARS and ROSEL. From the very beginning (e.g., patient recruitment) of these two studies to their termination and to the publication of research findings in the *Lancet*, I tried to examine this issue from a perspective of evidence-based medicine and avoid any preconception from my education training background that might exaggerates or underestimates the efficacy of this new technique. As we can image, these two studies were particularly challenging. For instance, it was impossible to recruit patients without supports from thoracic surgeons. Even so, patient recruitment remained difficult and slow in both two studies. Eventually only 58 patients were enrolled and the reasons could be complicated. Thus, the thoracic surgeons involved in these studies were great. They examined the lung cancer from the perspective of global cancer control rather than other considerations. In contrast, the views and opinions expressed by a small number of Chinese surgeons were quite disappointing and stunning. After the article was published in the *Lancet*, some doctors who were involved in lung cancer treatment found that they were affronted. Some thoracic surgeons even wrote articles without any solid evidence to criticize SABR, showing an unbelievable determination to kill this new technique in the cradle. However, the technological progression is an unstoppable and irreversible process. Today, video-assisted thoracoscopic surgery (VATS) has become one of the most important treatments for lung cancer, which was unimaginable three decades ago. However, any controversy or objection must be based on scientific evidences, not “take for granted”. I always support any evidence-based objection—it was these reasonable and justifiable objections that promoted the development of human technology.

Cancer is our common enemy. Cancer control requires the joint efforts of medical staff in surgery department, oncology department, radiotherapy department, pathology department, nursing department, and many other clinical and supporting departments. Lung cancer control remains challenging in China due to delayed and inadequate tobacco control and

environment (in particular air) pollution. According to the statistical data released by the National Cancer Center in 2015, lung cancer ranked the first in China in terms of both prevalence and mortality rate. Such a heavy disease burden reminds us all the time that lung cancer control requires the joint efforts of multiple disciplines, and different treatments from different disciplines are supporting rather than competing with each other. In contrast, the two studies published in the *Lancet* confirmed the effectiveness of SABR but did not deny the leading role of surgery in treating the early lung cancer. SABR should be a good supplement to surgical treatment. Thus, the lung cancer patients have a new choice and the doctors have a new weapon. Dr. Joe Y. Chang from the MD. Anderson Cancer Center was among the authors of this *Lancet* article. He wrote on social media, “*My suggestions are: first, we must be open to any criticism and try our best to carry out the ongoing RCTs; second, with a goal of achieving excellence, we must constantly improve the capability and quality of radiotherapy technology, so as to ensure the treatment effectiveness; and third, we must embrace the future by achieving the reasonable combination of chemotherapy, targeted therapy, radiotherapy, and immunotherapy. We shall remove professional boundaries and embrace new ideas, no matter whether such ideas come from chemotherapy, surgery, or radiotherapy. We must work together to fight against cancer, which is also a global dilemma.*”

I fully agree with Dr. Chang. While we must do a good job in our own field, we should also actively seek cooperation with other professionals, and such cooperation should not be confined to the areas of clinical medicine. As seen in the history of medicine, scientific&technological innovations and interdisciplinary cooperation have played decisive roles in the development of medicine. “Science and technology are the first productive force.” This is not a political slogan; rather, it is a universal truth that also applies medical science & technology. Without science and technology development during the Renaissance, medicine might remain in the era of traditional empirical medicine that was taught by word of mouth; without the advances in modern disciplines including physics, chemistry, biology, and materials science, the modern medicine might still wander between science and non-science. As we currently are in an era that the science & technology develops rapidly, we might be far left behind and even mislead our patients if we were too conservative to adopt new technology.

In view of the hot discussions on SABR and its potential therapeutic values, many journals under the AME Publishing House had invited 73 top thoracic surgeons and radiologists from 11 countries to share their insights on the subject of “Efficacy of SABR *vs.* Lobectomy in Treating Resectable Stage I Non-small cell Lung Cancer (NSCLC)”. This book is a collection of all these articles that may be particularly interested by our readers. The articles make detailed summaries of existing scientific evidences and clinical experiences, give objective elaboration on the current arguments, and shed light on future research directions and topics. The rich information in this book will for sure be valuable for all the colleagues who are engaged in lung cancer management. As always, any further comments on this topic will be warmly welcomed. As the publisher, we hope our subtle efforts will contribute to the fight against lung cancer.

Zhirui Zhou

Department of Radiation Oncology,

Tumor Hospital of Jilin Province,

Changchun, China;

Department of Radiation Oncology,

Fudan University Shanghai Cancer Center,

Shanghai, China