Improving Curative and Palliative Treatment Options in Lung Cancer with Focal Radiation, Part 1:
A Historical Perspective
by Dr. Vivek Mehta, Swedish Cancer Institute, Seattle, WA

Dr. West:
Hello, my name is Dr. Jack West. I'm a medical oncologist in Seattle Washington and the President and CEO of GRACE, the Global Resource for Advance in Cancer Education.

I’m happy to be here today with Dr. Vivek Mehta. Dr. Mehta is the Director of the Center for Advanced Targeted Radiotherapies at Swedish Cancer Institute, which is also where I work here in Seattle. He is a radiation oncologist with great expertise in these rapidly evolving topics of how best to treat lung cancer with some new, exciting technologies that are being used in some cases as a new treatment option for previously treated patients, for patients with metastatic disease, and also potentially as an alternative to surgery for patients with earlier stage disease.

So, potentially a curative therapy, potentially as a palliative therapy. He’ll be talking about all of these issues.

He’s also the Vice-President of GRACE and has been participating in the leadership of GRACE, in that role, over the last several years.

I’d like to thank the LUNGevity Foundation for partnering with GRACE and making this webinar and this entire series of webinar programs possible.

At this point, I’m going to just turn it over to Dr. Mehta and thank him for joining us today.

Dr. Mehta:
Thank you, Dr. West, for those kind words. It’s my pleasure to talk to you a little about some of the advances in radiation, particularly as it applies to the treatment of patients with lung cancer. With that in mind, I’ll plan on getting started right now.

We’re talking to you from the Cancer Institute here at the Swedish Hospital. We call it Swedish Cancer Institute. As many of you know this was founded back more than 75 years ago, it’s the oldest cancer institute west of the Mississippi. We’ve got a long track record of innovation and development within radiation oncology. You’re looking at some pictures from the very first machines that were actually installed here in this department.

With that as a backdrop, I wanted to switch gears and start talking to you a little bit about early stage lung cancer. There are more than 175,000 patients that are diagnosed with early stage disease each year. Out of that 175,000 cases, only a few of them are actually early stage. When we talk about what early stage means, that generally means a small primary tumor that hasn’t spread to lymph nodes that are far away, or if they have spread to lymph nodes they’re on close proximity and it certainly hasn’t spread to other tissues in the body.
For these patients, with early stage, small, localized disease, surgery has often been considered the gold standard – or what we’ve done for years or decades now. That standard surgery is typically the removal of an entire lobe of the lung. If you look at the studies, most studies suggest that when you do that surgery, you cure about 50% to 70% of the patients with early stage disease.

Lung cancer, however, is often found in patients that are considered medically inoperable. What we mean by that is maybe they have a bad heart or their lungs are simply not good enough to go through an operation. Maybe they’re not good enough to have the anesthesia, maybe they’re not good enough to go through the taxing toll of an operation, or maybe they simply won’t have enough lung function left after the operation to be considered functional.

Patients that fall into this category are sometimes simply followed. Sometimes, they’re never sent because they simply have too many other medical problems.

Historically, some of these patients that are medically inoperative found their way to radiation oncologist and were treated with radiation. The classic way of treating these patients was with what we call fractionated radiotherapy, which is a low dose of radiation that's delivered Monday through Friday.

Typically, the treatments go for six to seven weeks, somewhere they've had 30 or 35 visits occur. The total dose these patients receive is somewhere between 60 and 70 gray. Gray is the unit of calculation for radiation that we typically use so that we can crosstalk among different platforms and different centers. Typically, they’re receiving about 2 gray per fraction each day.

The reason that we have given radiation in that manner – as a low dose every day, Monday through Friday over a period of several weeks – has really evolved from some rationale that we learned from investigations and in Petri dish sort of experiments if you will. If I were to generalize that, I would say that it's evolved as an effort to try to reduce the toxicity that somebody receiving the radiation would experience.

So, if you give it as a low dose every day and you continue to give it over that period of seven weeks, you’re allowing the normal tissues to try to repair themselves from that injury. The tumor cells, however, because they’re going so rapidly and lack that ability to repair are not affected by the low dose necessarily. They simply get the effect of the radiation and get that damage. But the normal tissues, since they’re not growing as rapidly and have this ability to repair, can repair that effect.

It usually takes about four hours for a normal tissue to repair that effect. So, by spacing the radiation treatments out on a day-to-day basis with 24 hours between them, you’re giving the normal cells more than six times than the time they need to repair that injury. The reason that we gave this low dose, Monday through Friday for seven weeks was to try to spare both the short term and long term side effects associated with the treatment.

The normal tissue toxicity is dependent on the total dose and the overall treatment time. Dividing that dose into these multiple fractions, allow the ability for re-oxygenation, redistribution, re-assortment, repopulation and damage repair; the biological processes that are going on at the cellular level that facilitate normal cells from healing up and exploit a difference between the normal cell and the cancer cell.
What you’re looking at right now is a chest x-ray. In the upper left-hand field, you can see a square box. That square box is meant to highlight a cancer that’s in this particular patient. The cancer is the roundest density that you see in that area. Classically, these radiotherapy fields that were used to treat patients were based on those chest x-rays. The orientation of the fields flows front to back and a square box is used.

In fact, a lot of people refer to this sort of treatment as what we call the postage-stamp treatment. What you see right here is a classic postage stamp, a square box being applied. The radiation will come from the front and the back of the patient while they’re lying on the table and it would treat everything in the middle, and in the middle includes the cancer that we’re talking about.

If you go back through the literature and you try to figure out how good we did with this particular technique, this conventional radiation for these early stage lung cancers, here’s a series of publications that have been done. The range of doses, like I said, somewhere in the 60 to 70 range. You can see that controlling the disease locally was somewhere between 30% and 80%.

One of the things that you will notice is that the percentages of local control that are higher are often associated with higher doses of radiation. But a ballpark number, using this particular treatment approach, we were able to control a local tumor about 50% of the time.

If I were to summarize the standard conventionally fractionated approach for this disease, I would tell you that what we learned over the years is that if you can give higher doses, you’re more likely to control the tumor.

If the tumor is large even though it’s early stage, meaning greater than two centimeters, it’s going to require higher doses to sterilize all the cells. If it’s smaller, less than two centimeters, our outcomes are better because we’re sterilizing more of the cells even if we use a lower dose. The last thing I would tell you is that most of the published reports in this particular group of patients uses older techniques and treated in an era that’s not quite the same as the era that we practice in medicine today; they didn’t have the same staging, same technology, same treatment approaches.

If you try to compare this conventional radiotherapy approach to surgery – and it’s impossible not to want to do that because in the surgical approach you subject yourself to a big operation and a lobe of your lung is removed. In this approach, you don’t have nearly the same surgical procedure going on. You lay on a table and you get daily radiation. You will come to the conclusion, and as much as I hate to admit this, that the surgical series are probably better than conventional radiation.

Surgical series generally report about a 10% better survival than radiotherapy conventionally-treated patients report. There are some difficulties in comparing this because when the surgeon operates he gets an exact tumor measurement where the radiation oncologist delivers the radiation. He’s using it based on a chest x-ray or a CT scan.

There’s a difference between having the pathologic data and using that to define the stage of the patient and the clinical data. More importantly, I think one of the reasons that we shouldn’t be comparing at least these groups of patients is that classically the patients that got radiation were not the patients that were eligible for surgery. So, we weren’t really comparing apples to apples, if you will.