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SUCCESSFUL TREATMENT OF CHEMOTHERAPY AND RADIOTHERAPY FOR LUNG CANCER USING MATHEMATICAL MODEL

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Abstract:

Chemotherapy simply means treatment with chemicals. Those used to treat cancer are called cytotoxic drugs because they poison cells in the body. Chemotherapy drugs are carried by the bloodstream throughout the body. The drugs affect both normal healthy cells and cancerous ones. However, healthy cells are able to repair themselves. Most types of chemotherapy for lung cancer are given directly into vein through a drip (intravenously). However, there are some types of chemotherapy which are given as a tablet. If the small cell lung cancer (SCLC), chemotherapy is usually the first type of treatment. The other method is internal radiation therapy. This method is also called brachytherapy. Internal radiation therapy involves placing a radioactive object for lung cancer internal radiation can shrink a blocking. Radiation is given through a plastic tube that is inserted into the removed after the treatment session. Using Poisson process, we studied the Continuous improvement of the health in the various stages of Chemotherapy and Radiotherapy treatments.

Key Words: SCLC, Oncology, EBRT & Cancer Stem Cells

1. Introduction:

Lung cancer, also referred to as bronchogenic carcinomas, is a major contributor in the United States. The development of lung cancer occurs on the lining glands, which contains damage cells that are located in our lungs and bronchial air ways known as the tracheobronchial system [9]. This part of human being is important because this system is susceptible to being contaminated by inhaled, air which is a major cause of lung cancer. The major cause of lung cancer is due to cancer-causing agents known as carcinogens, such as asbestos and radon. However, research and statistics show that the major agent of lung cancer is tobacco smoke, which contains over 60 carcinogens.

Now a day, cigarette smoke is responsible for a great proportion of deaths within tobacco smoke. Each year, in U.S.A the approximately 400,000 people die from cigarette smoke, which accounts for one in every five deaths in U.S.A. [6]. The likelihood that a smoker will develop lung cancer from cigarette smoke depends on many aspects like: the age at which smoking began. How long the person has smoked. The number of cigarettes smoked per day, and how deeply the smoker inhales [1]. The relationship between cigarette smokes with respect to lung cancer has been established in 85-90 percent of all lung cancer cases (1, 46,000 case/year). Furthermore, an estimated 3,000 non-smoker die per day from lung cancer due to second-hand smoke (also known as environmental tobacco smoke)[6]. The number of deaths of non-smokers may be lower than active smokers, but according to the U.S.A. Environmental protection agency, it is quite large when compared to those associated with other indoor and outdoor environmental pollutants. This data has had a great impact on public policies that protect people from second hand-smoke [2]. Based on the relationship between lung cancer and cigarette smoke, we want to show the reduction between non-smokers and smokers, and how to decrease the rate in which nonsmokers and smokers progress towards lung cancer.

However, the best way to detail the transition of each class is to use a mixture of parameters, probabilities, and rates. Based on the behavior of each class, the Poisson process is created. One of the main purposes of the distribution is to obtain the sample points. This is used to find the basic reproductive number, which represents the rate that people get cured. Through simulations, the model is analyzed to obtain different situations that produce interesting

results among the specific classes.

Smoking in public, places was prohibited nationwide from 2nd oct. 2008. There are approximately 120 million Smokers in India. India is home to 12% of the world's Smokers. More than 1.5 million people die every year due to tobacco related problem [10]. And 35% adult in India consume tobacco in some form and 32% of India male and 19% of female are exposed to second hand Smoke [9].

Chemotherapy:

Many reasons are behind giving chemotherapy treatment for Lung cancer. These include:

- ✓ Cure early stage inoperable lung cancer in combination with radiotherapy (chemotherapy).
- ✓ Extend length of life when a cure is not possible (palliative).
- ✓ Remove any cancer cells which may still exist after surgery for lung cancer (adjuvant).
- ✓ Reduce symptoms, such as breathlessness (palliative).

Chemotherapy for Small Cell Lung Cancer:

The chemotherapy drugs used for small cell lung cancer are usually given through a vein as an intravenous IV infusion. Chemotherapy is usually given during a treatment period called a cycle. For small cell Lung cancer a single cycle lasts about three or four week and consists of an IV infusion for several hours each day, for a few days in one week, followed by a period of rest [7]. Limited – Stage Small cell Lung cancer, combination Chemotherapy plus radiation therapy given at the same time is the recommended treatment. The most commonly used initial Chemotherapy regimen is topside (toposar or vepesid) plus cisplatin (platinol) known as EP [7]. Extensive – stage small cell Lung cancer, Chemotherapy alone using the EP regimen is the standard treatment. However, another regimen that may be used is carboplatin (paraplatin) plus irinotecan (camptosar) [7]. These include:

- ✓ The type (pathology) of lung cancer you have.
- ✓ The size, position and spread of your lung cancer (stage).
- ✓ The general health and how will cope with treatment.

Radiation Therapy:

At high doses, radiation therapy kills cancer cells or slows their growth by damaging their DNA. Cancer cells whose DNA is damaged beyond repair stop dividing or die they are broken down and removed by the body. Radiation therapy does not kill cancer cells right away. It takes days or weeks of treatment before DNA is damaged enough for cancer cells to die [3].

Internal Radiation:

Internal radiation is also called brachytherapy. Internal radiation therapy uses a radiation source that's usually sealed in a small holder called an implant. The implant is placed very closed to or inside the tumor, so that it harms as few normal cells as possible. Internal radiation therapy allows a higher dose of radiation in a smaller area than might be possible with external radiation treatment [8].

Simulation:

Treatment planning with a simulation session is needed. During simulation, pictures of the tumor will be taken with an imaging test. Pictures are taken after your body is moved into the position needed for treatment. The CT scans within 4 weeks of treatment are advised. If your breathing causes large movements, motion control methods during the scans may be used [4].

External Radiation:

External Beam radiation therapy (EBRT) focuses radiation from outside the body on the cancer. This is the type of radiation therapy most often used to treat NSCLC or its spread to other organs. Most people have external beam radiation therapy once a day, five days a week, Monday through Friday. Treatment lasts anywhere from 2 to 10 weeks, depending on the type of cancer and the goal of the treatment [3].

Low-Dose Rate (LDR) Implants:

LDR brachytherapy usually involves placement of radioactive sources at the tumor bed during surgical resection of the tumor. These radioactive sources deliver radiation therapy at the rate of ~2 Gy / hour [8].

2. Mathematical Modeling:

Here we deal with stochastic process in continuous time and with discrete state space, process. In this process consider a random event E such as Chemotherapy and Radiotherapy treatment given to the cancer patients. Let us consider the total number N (t) of occurrences of the event E in an interval of duration t. Here the values of N (t) are observed valued of the random variable N(t). Let p_n (t) be the probability that the random variable N (t) assumes the value in [5]. i.e., $p_n(t)=p_r\{N(t)=n\}$.This Probability is a function of the time t. Since the only possible values of n are n = 0, 1, 2,…. $\sum_{n=0}^{\infty} p_n = 1$, thus,$\{p_n(t)\}$ represents the probability distribution of the random variable N (t) for every value of t. The family of random variable {N (t), t≥0} is a stochastic process. Here the time t is continuous, the state space of N(t) is discrete and integral-valued and the process is integral-valued. The probability distribution $\{p_n(t)\}$ of N (t) is given by

$P_n(t) = \frac{e^{-\lambda t}(\lambda t)^n}{n!}$, n = 0, 1, 2, 3… and mean = E {N (t)} = λ t, Variance {N (t)} = λ t.

If x is a random variable which can assume any one of the values $x_1, x_2, \ldots, x_n$ With respective probabilities $p_1, p_2, \ldots, p_n$ Then the mathematical expectation of x, usually called the expected value of x and denoted by E(x) $= p_1x_1 + p_2x_2 + \ldots + p_nx_n$, where more precisely. If x is random variable with probability distribution $\{x\ p(x)\}$ then,

$$E(X) = \sum xp(x)$$

The above summation being taken over different values of *x*. Let us consider the following frequency distribution of the random variable *x*. X: $x_1, x_2, x_3 \ldots x_i \ldots x_n$ and F: $f_1, f_2, f_3 \ldots f_i \ldots f_n$. Then the mean of the distribution is given by

$$\bar{x} = \frac{f_1x_1 + f_2x_2 + \cdots + f_nx_n}{N} \quad \text{i.e,} \quad \bar{x} = \frac{\sum_i f_i x_i}{N}$$

There are 15 Lung cancer patients have been selected and gave chemotherapy and radiotherapy treatment. For each patient Cisplatin 50mg and radiation 50.4 Gy has been given for 5 days in a week (Monday to Friday) which is continued for 5 weeks. The health improvement of those patients are considered as probability values at the given time interval. Here, treatment given to patient is the event E and n=15. Mean E {N (t)} =100. The process N (t) is related to the event E (giving Chemotherapy and radiotherapy) and the improvement of the health condition is the outcome which was given in the table. The outcome of this treatment is good, especially if the cancer is in earlier stage. The cancer is 100% curable by using this chemotherapy and radiotherapy.

The Lung Cancer Patients treatment details are given in the below table:

Table 1: Chemotherapy Treatment at first week

N	Valid	15
	Missing	0
Mean		41.4667
Std. Deviation		1.35576

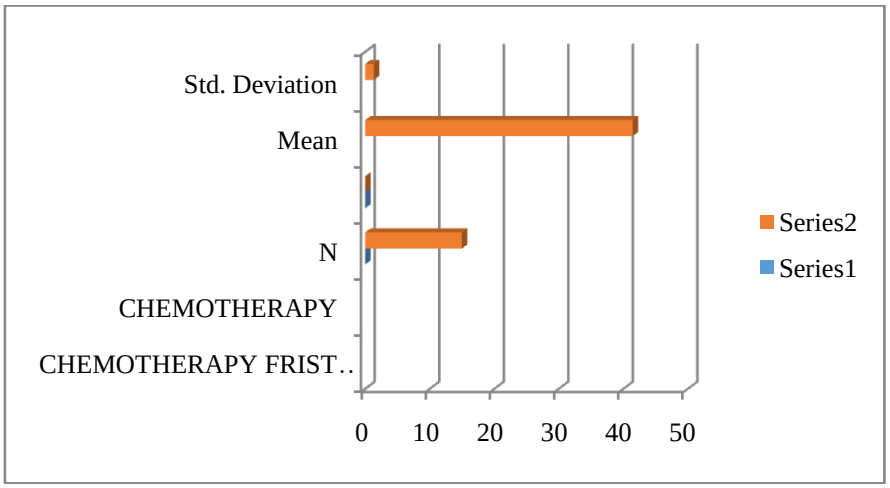

Figure 1: Showing chemotherapy treatment at first week

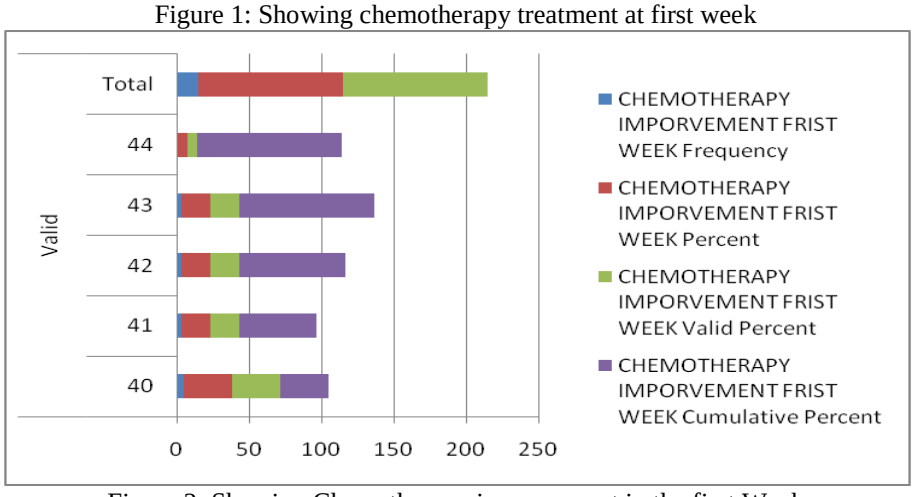

Figure 2: Showing Chemotherapy improvement in the first Week

When chemotherapy treatment is given for 5 patients, they receive 40% of improvement and 33.3% of cumulative percentage and given to 3 patients, the result of improvement is 41% and cumulative percentage is 53.3% and given to 3 patients, the improvement of treatment is 42% and cumulative is 73.3%.Where as treatment given to 3 patients again the percentage of improvement of treatment is 43% and cumulative percentage is 93.3% and finally treatment given to 1 patient the improvement is 44% and cumulative percentage is 100%.

Table 2: Showing Radiotherapy treatments at first week

		Radio 01	Radio 02	Radio 03	Radio 04
N	Valid	15	15	15	15
	Missing	0	0	0	0
Mean		35.8667	41.8	45.2667	49.3333
Std. Deviation		1.24595	1.61245	1.62422	0.89974

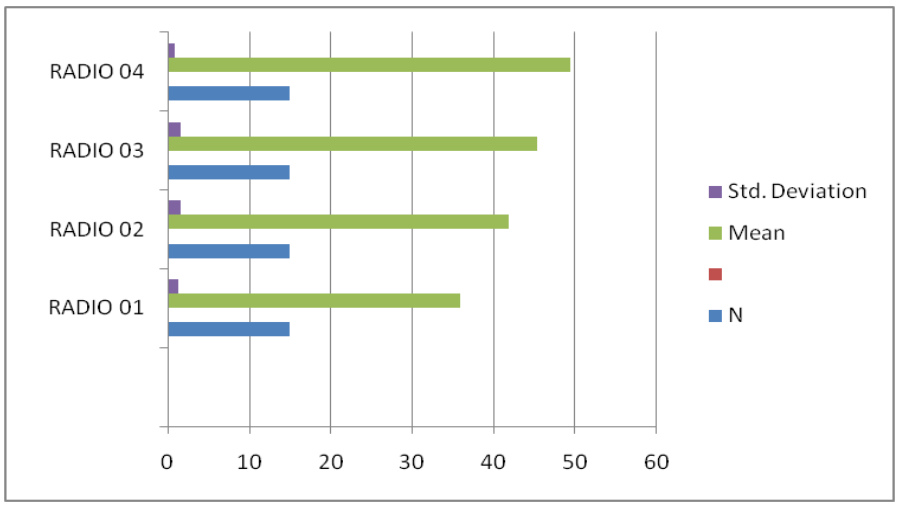

Figure 3: Showing Radiotherapy treatments at first week

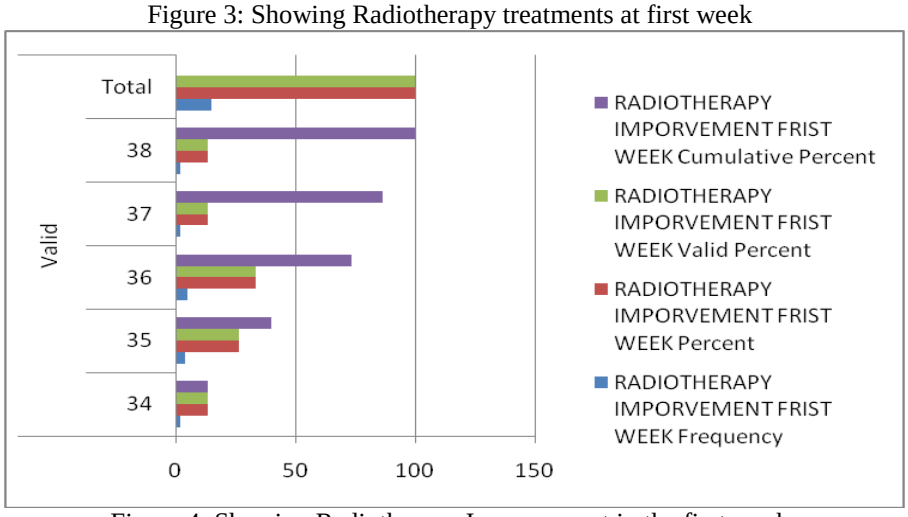

Figure 4: Showing Radiotherapy Improvement in the first week

When Radiotherapy treatment is given for 2 patients they receive 34% of improvement and 13.3% of cumulative percentage and treatment given to 4 patients, the result of improvement is 35% and cumulative percentage is 40% and given to 5 patients, the improvement of treatment is 36% and cumulative percentage is 73.3%.Where as treatment given to 2 patients again the percentage of improvement of treatment is 37% and cumulative percentage is 86.7% and finally treatment given to 2 patients, the improvement is 38% and cumulative percentage is 100%.

Table 3: Chemotherapy treatments at second week

Chemotherapy 2nd Week		
Chemotherapy		
N	Valid	15
	Missing	0
Mean		56
Std. Deviation		1.4142

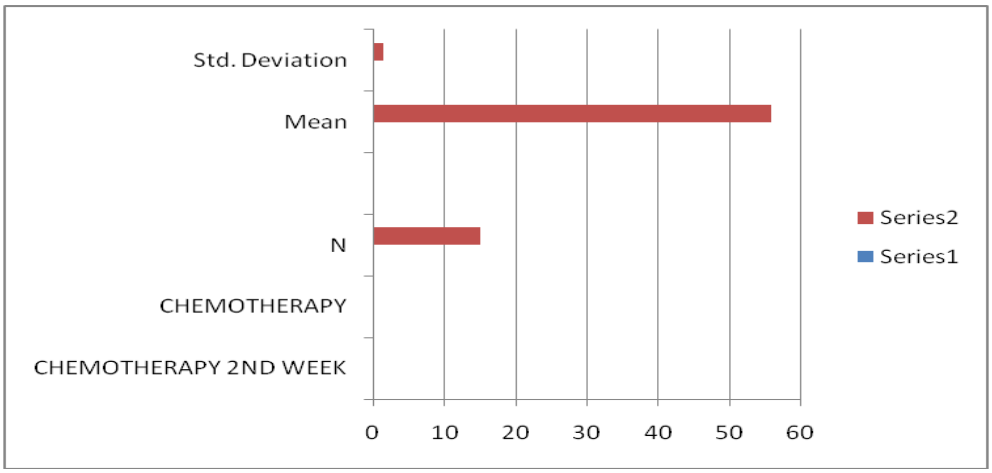

Figure 5: Showing Chemotherapy treatments at second week

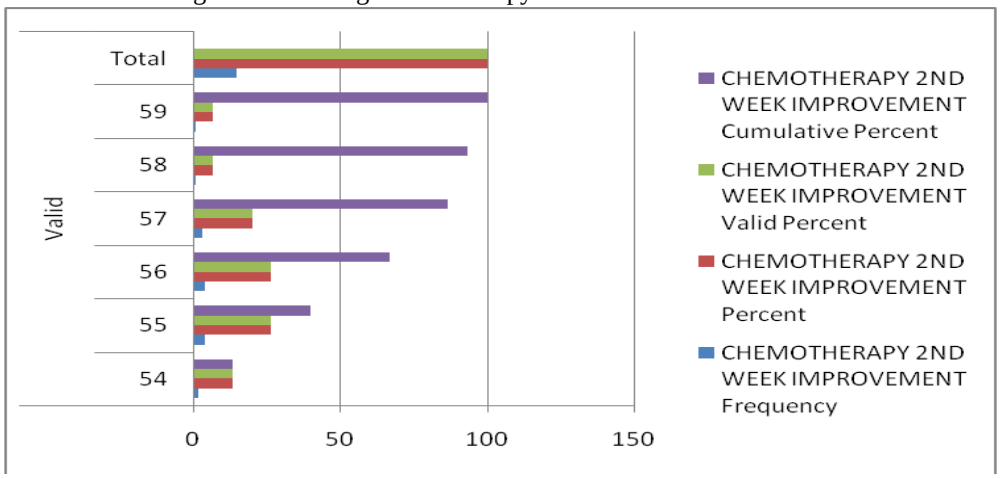

Figure 6: Showing Chemotherapy improvements in the second week

When chemotherapy treatment is given for 2 patients they receive 54% of improvement and 13.3% of cumulative percentage and treatment given to 4 patients, the result of improvement is 55% and cumulative percentage is 40% and given to 4 patients, the improvement of treatment is 56% and cumulative is 66.7%.Where as treatment given to 3 patients again the percentage of improvement of treatment is 57% and cumulative percentage is 86.7% and given 1 patient the result of the improvement of treatment 58% and cumulative is 93.3% and finally treatment given to 1 patient the improvement is 59% and cumulative percentage is 100%.

Table 4: Radiotherapy treatments at second week

Radiotherapy 2nd Week					
		Radio 05	Radio 06	Radio 07	Radio 08
N	Valid	15	15	15	15
	Missing	0	0	0	0
Mean		56.4	58.5333	63.4667	64.7333
Std. Deviation		1.72378	0.74322	1.24595	0.45774

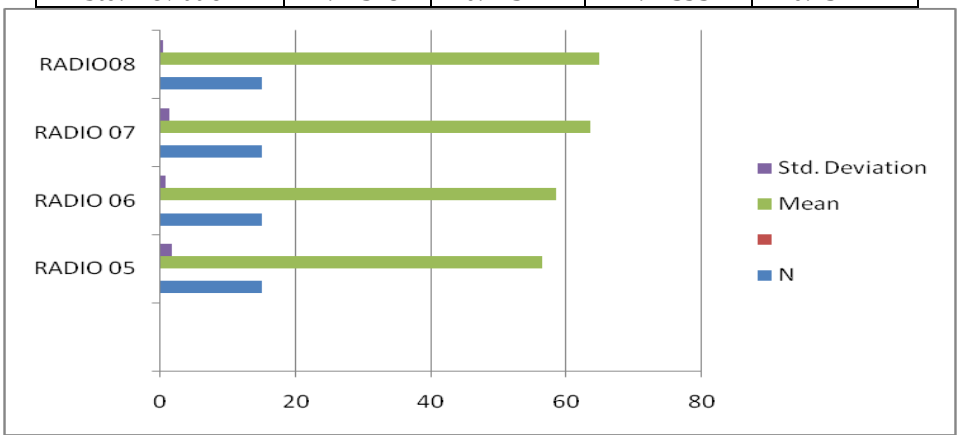

Figure 7: Showing Radiotherapy treatments at second week

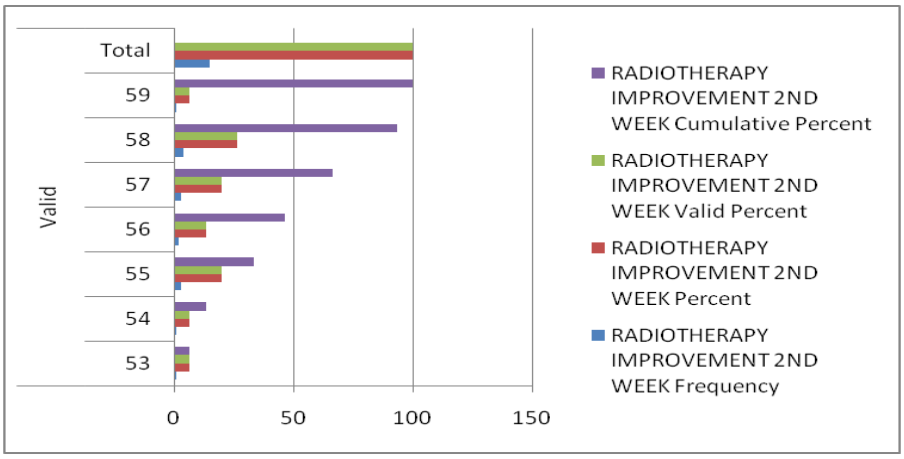

Figure 8: Showing Radiotherapy improvements in the second week

When Radiotherapy treatment is given for 1 patient they receive 53% of improvement and 6.7% of cumulative percentage given to 1 patient, the result of improvement is 54% and cumulative percentage is 13.3%. and given to 3 patient, the improvement of treatment is 55% and cumulative is 33.3%.Where as treatment given to 2 patients again the percentage of improvement of treatment is 56% and cumulative percentage is 46.7% and given to 3 patient the result of the improvement of treatment 57% and cumulative is 66.7% and given to 4 patient, the improvement of treatment is 58% and cumulative 93.3% and finally treatment given to 1 patient the improvement is 59% and cumulative percentage is 100%.

Table 5: Chemotherapy Treatment at third week

Chemotherapy 3rd Week		
Chemotherapy		
N	Valid	15
	Missing	0
Mean		63.0667

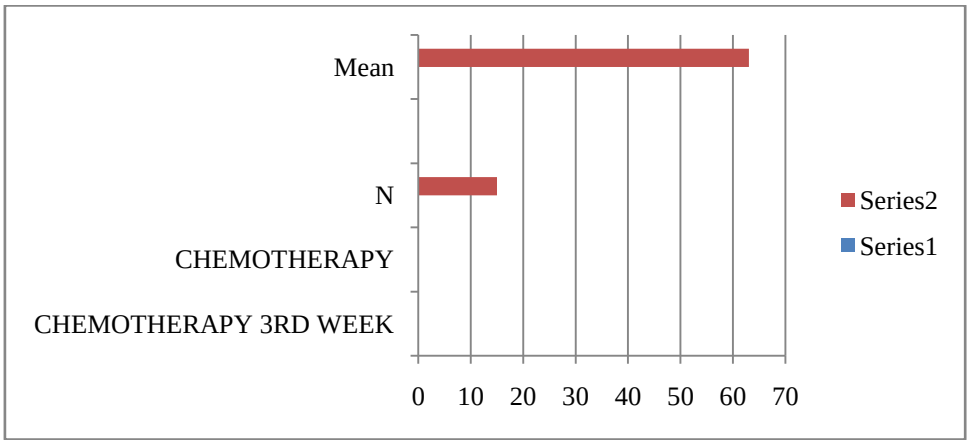

Figure 9: Showing Chemotherapy Treatments at third week

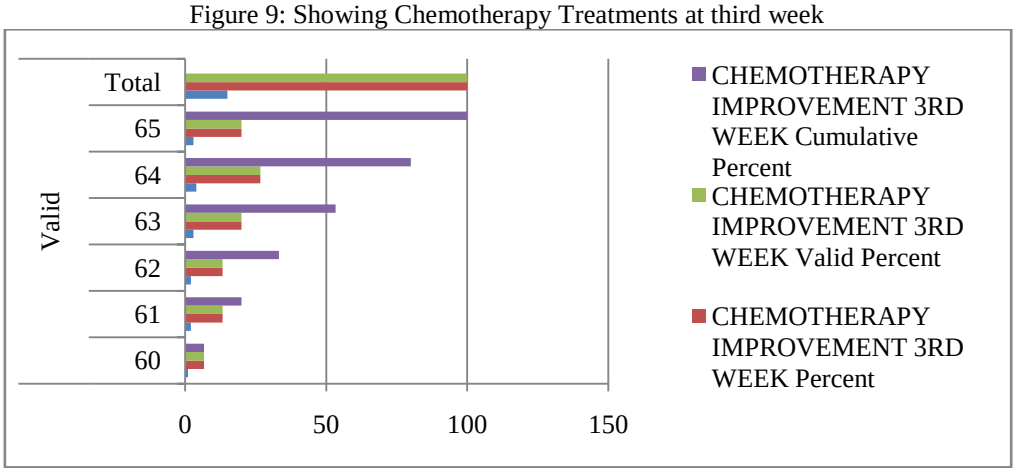

Figure 10: Showing Chemotherapy Improvements in the third week

When Radiotherapy treatment is given for 1 patient they receive 60% of improvement and 6.7% of cumulative percentage and treatment given to 2 patients, the result of improvement is 61% and cumulative percentage is 20% and given to 2 patients, the improvement of treatment is 62% and cumulative is 33.3%.Where as treatment given to 3 patients again the percentage of improvement of treatment is 63% and cumulative percentage is 53.3% and given 4 patients the result of the improvement of treatment 64% and cumulative is 80% and finally treatment given to 3 patients, the improvement is 65% and cumulative percentage is 100%.

Table 6: Radiotherapy treatments at third week

Radiotherapy 3rd Week					
		Radio 09	Radio 10	Radio 11	Radio 12
N	Valid	15	15	15	15
	Missing	0	0	0	0
Mean		63.8	65.4	67	67.8667
Std. Deviation		0.94112	1.18322	1.73205	0.91548

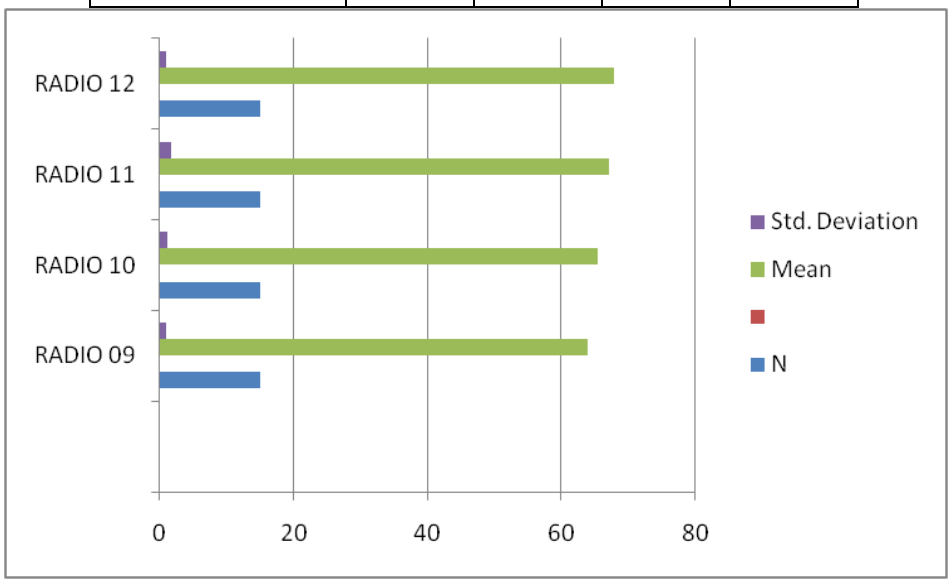

Figure 11: Showing Radiotherapy treatment at third week

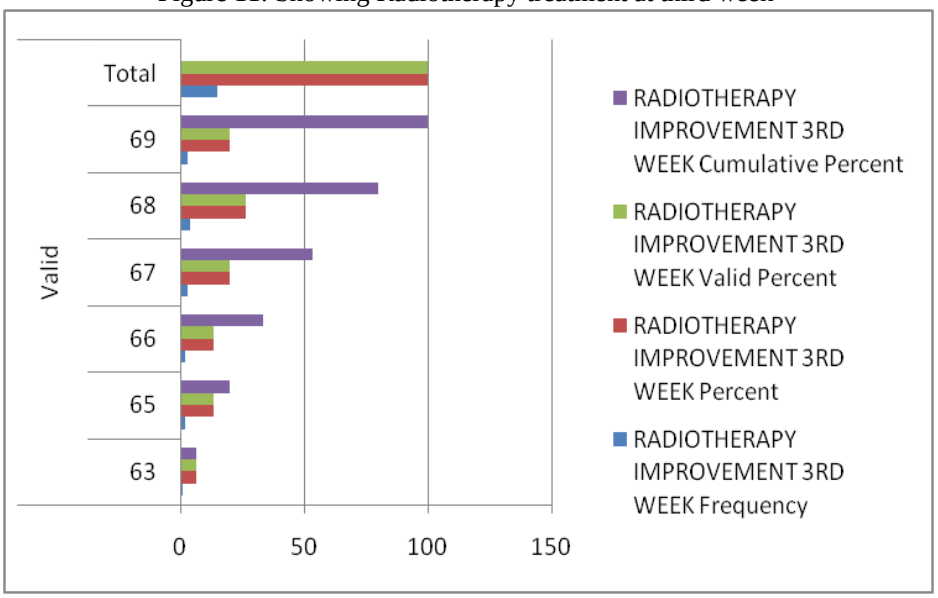

Figure 12: Showing Radiotherapy improvements in the third week

When Radiotherapy treatment is given for 1 patient they receive 63% of improvement and 6.7% of cumulative percentage and treatment given to 2 patients, the result of improvement is 65% and cumulative percentage is 20% and given to 2 patients, the improvement of treatment is 66% and cumulative is 33.3%.Where as treatment given to 3 patients again the percentage of improvement of treatment is 67% and cumulative percentage is 53.3% and given 4 patients the result of the improvement of treatment 68% and cumulative is 80% and finally treatment given to 3 patients, the improvement is 69% and cumulative percentage is 100%.

Table 7: Chemotherapy treatments at fourth week

Chemotherapy 4th Week		
Chemo		
N	Valid	15
	Missing	0
Mean		76.6
Std. Deviation		1.80476

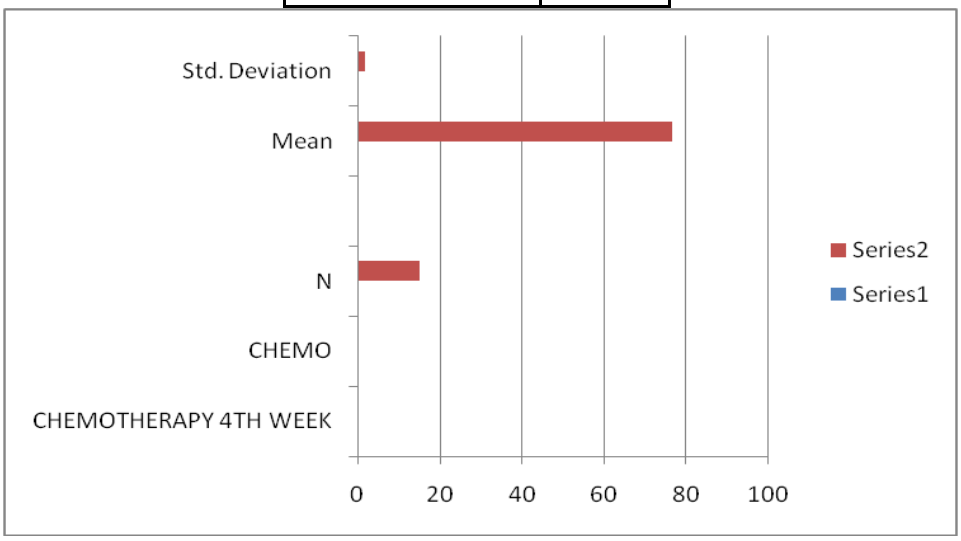

Figure 13: Showing chemotherapy treatment at fourth week

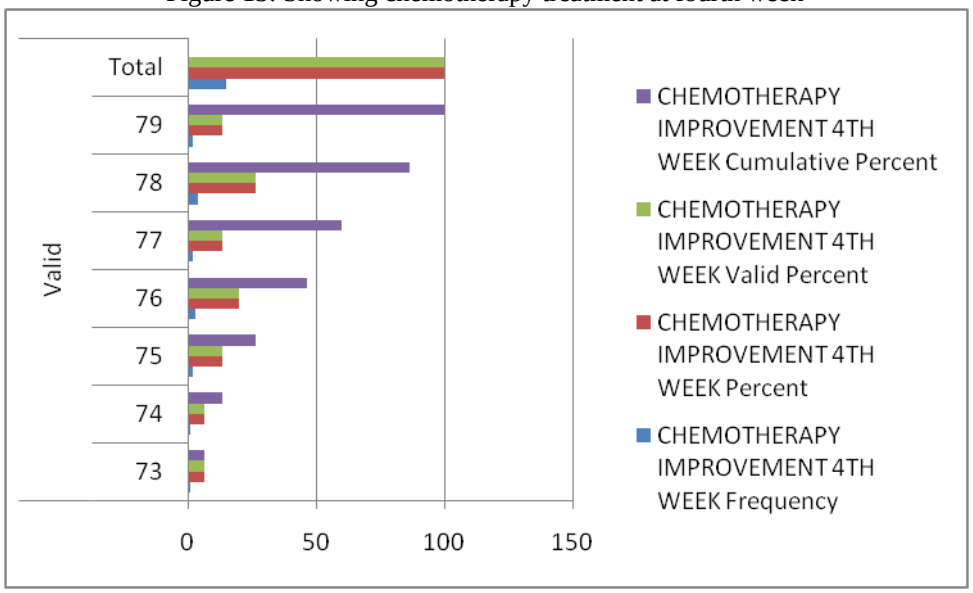

Figure 14: Showing Chemotherapy improvements in the fourth week

When chemotherapy treatment is given for 1 patient they receive 73% of improvement and 6.7% of cumulative percentage and treatment given to 1 patient, the result of improvement is 74% and cumulative percentage is 13.3% and given to 2 patients, the improvement of treatment is 75% and cumulative is 26.7%.Where as treatment given to 3 patients again the percentage of improvement of treatment is 76% and cumulative percentage is 46.7% and given to 2 patients the result of the improvement of treatment 77% and cumulative is 60% and given to 4 patients, the improvement of treatment is 78% and cumulative 86.7% and finally treatment given to 2 patients, the improvement is 79% and cumulative percentage is 100%.

Table 8: Radiotherapy treatments at fourth week

Radiotherapy 4th Week					
		Radio 13	Radio 14	Radio 15	Radio 16
N	Valid	15	15	15	15
	Missing	0	0	0	0
Mean		76.4667	84.0667	86.9333	88.1333
Std. Deviation		1.35576	2.15362	1.09978	0.83381

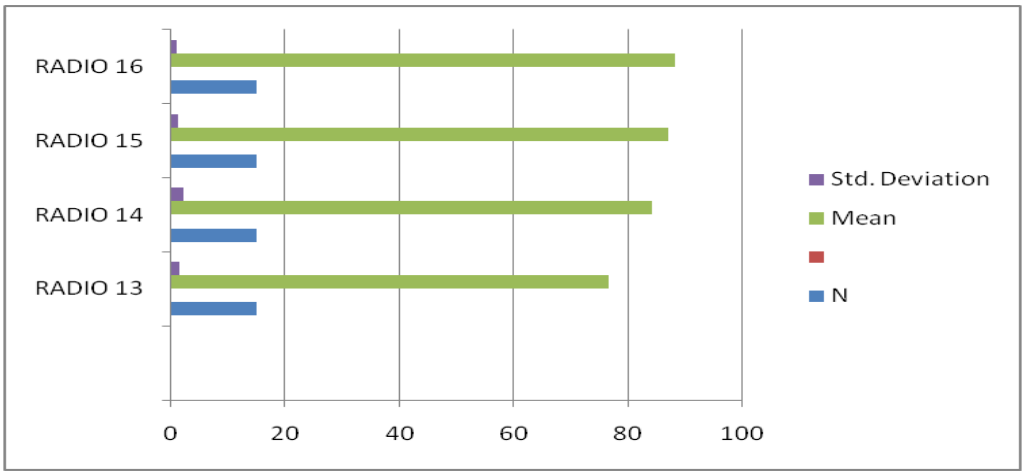

Figure 15: Showing Radiotherapy Treatment at Fourth week

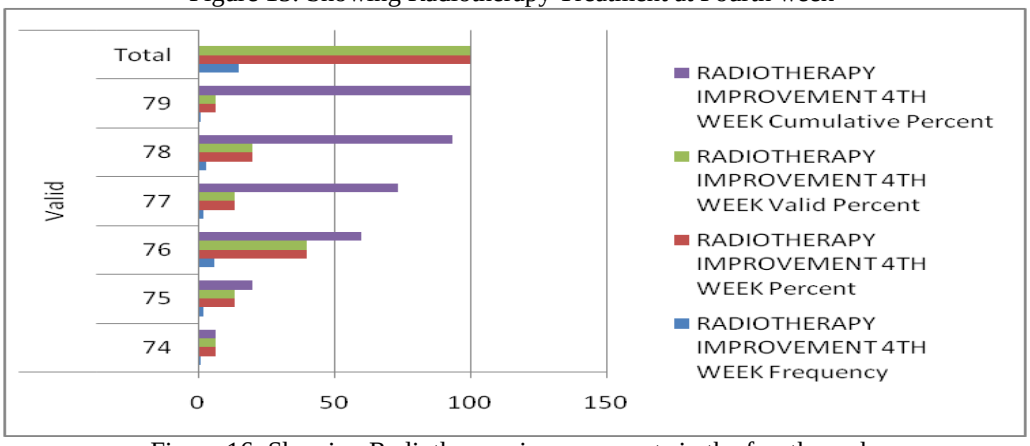

Figure 16: Showing Radiotherapy improvements in the fourth week

When Radiotherapy treatment is given for 1 patient they receive 74% of improvement and 6.7% of cumulative percentage and treatment given to 2 patients, the result of improvement is 75% and cumulative percentage is 20% and given to 6 patients, the improvement of treatment is 76% and cumulative is 60%.Where as treatment given to 2 patients again the percentage of improvement of treatment is 77% and cumulative percentage is 73.3% and given to 3 patients the result of the Improvement of treatment 78% and cumulative is 93.3% and finally treatment given to 1 patient, the improvement is 79% and cumulative percentage is 100%.

Table 9: Chemotherapy Treatment at fifth week

Chemotherapy 5th Week		
Chemo		
N	Valid	15
	Missing	0
Mean		92.2667
Std. Deviation		1.79151

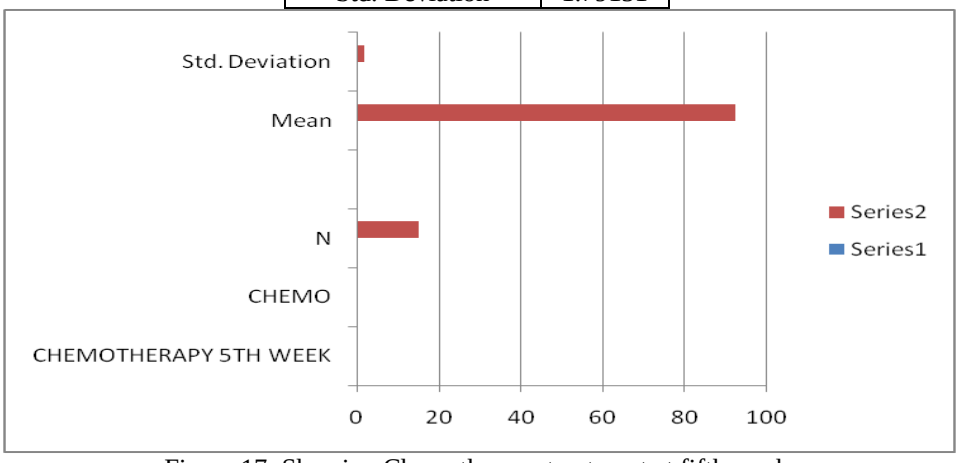

Figure 17: Showing Chemotherapy treatment at fifth week

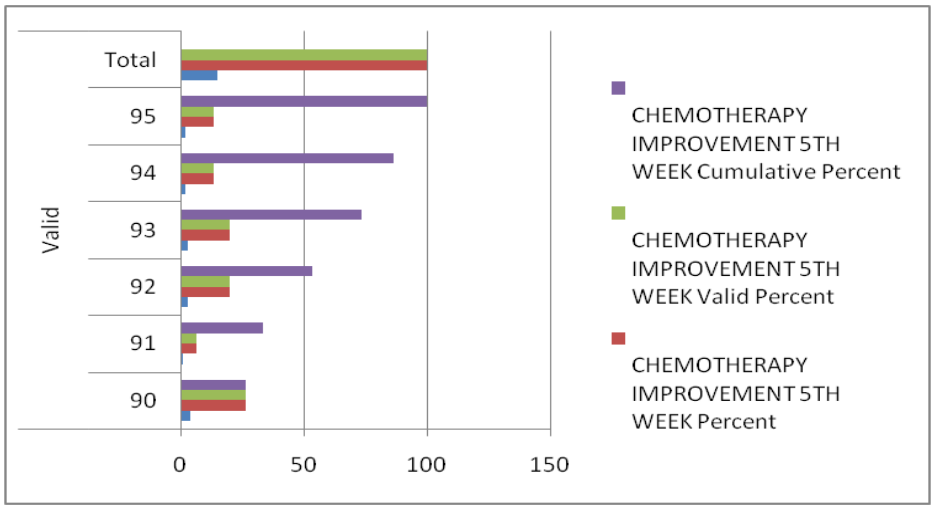

Figure 18: Showing Chemotherapy improvements in the fifth week

When chemotherapy treatment is given for 4 patients, they receive 90% of improvement and 26.7% of cumulative percentage and treatment given to 1 patient, the result of improvement is 91% and cumulative percentage is 33.3% And given to 3 patients, the improvement of treatment is 92% and cumulative is 53.3%.Where as treatment given to 3 patients again the percentage of improvement of treatment is 93% and cumulative percentage is 73.3% and given to 2 patients the result of the improvement of treatment 94% and cumulative is 86.7% and finally treatment given to 2 patients, the improvement is 95% and cumulative percentage is 100%

Table 10: Radiotherapy Treatment at 5th week

		Radio 17	Radio 18	Radio 19	Radio 20
N	Valid	15	15	15	15
	Missing	0	0	0	0
Mean		93.4667	92.7333	94.2667	93.3333
Std. Deviation		1.99523	2.40436	1.0328	1.1127

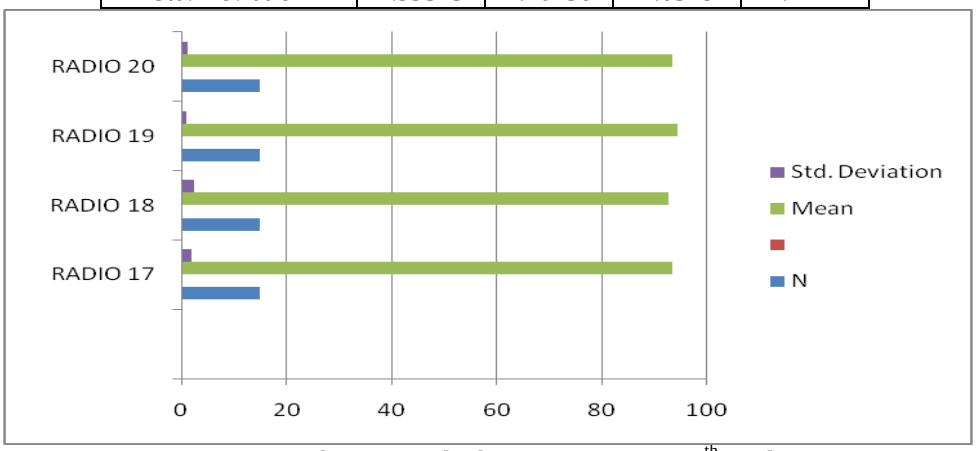

Figure 19: Showing Radiotherapy treatment at 5th week

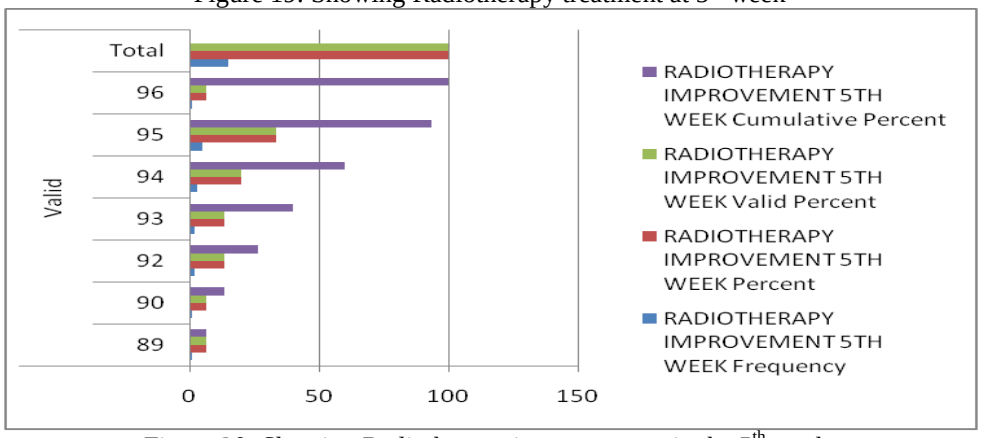

Figure 20: Showing Radiotherapy improvements in the 5th week.

When Radiotherapy treatment is given for 1 patient, they receive 89% of improvement and 6.7% of cumulative percentage and treatment given to 1 patient, the result of improvement is 90% and cumulative percentage is 13.3% And given to 2 patients, the improvement of treatment is 92% and cumulative is 26.7%.Where as treatment given to 2 patients again the percentage of improvement of treatment is 93% and cumulative percentage is 40% and given to 3 patients, the result of the improvement of treatment 94% and cumulative is 60% and given to 5 patients, the improvement of treatment is 95% and cumulative 93.3% and finally treatment given to 1 patient, the improvement is 96% and cumulative percentage is 100%

Conclusion:

By this analysis the treatment of chemotherapy and Radiotherapy had been given continuously for five weeks. We given that, the early stage of lung cancer getting complete cured and the others improvement in health level. Chemotherapy and Radiotherapy treatment is one of the best treatments for lung cancer among other treatment. At the same time least number of side effects has been acknowledged by the patients when they got Chemotherapy and Radiotherapy treatment.

Acknowledgement:

The doctors and Management of GVN Hospital, Trichy had supported in many ways to do this study. In Particular a number of experts give the ideas and suggestion about lung cancer etc. And also I met patients with many questions for collecting data.

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