EARLY LUNG CANCER DETECTION USING COMPUTED TOMOGRAPHY

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INTRODUCTION
Lung cancer is the leading cause of cancer-related death in United States and worldwide with around 1.3 million death per year. But general prognosis of lung cancer is poor. Overall, 16% of people in the United States diagnosed with lung cancer survive five years after the diagnosis [1]. Late diagnosis is the primary reason for the high mortality. Lung cancer is assigned a stage from I to IV in order of severity. Stage is often advanced at the time of diagnosis. At presentation, 30-40% of cases of non-small cell lung cancer (NSCLC) are stage IV, and 60% of SCLC are stage IV. Higher-stage cancers generally have a worse prognosis than lower-stage cancers [2]. If lung cancer can be detected early, the survival rate can be improved significantly.

Existing imaging tests for lung cancer detection include Positron Emission Tomography(PET), Magnetic Resonance Imaging (MRI) and Chest X-Ray. Young et al. have reported that positron emission tomography suffers the problem of low resolution and high false positives. As for MRI, Collette et al.’s research points out that people with metal implants in their body may not be able to have a MRI performed. Because MRI is done using a very strong magnetic field which is possibly move the metal parts in the body [3]. Chest X-Ray has similar problems as PET and it’s not sensitive enough due to Fred et al.’s research. Besides imaging test, lung biopsy is also used. A biopsy is a procedure in which a small tissue sample is removed from the nodule so it can be examined under a microscope. It’s usually invasive and painful. As compared to these traditional tests, Computed Tomography (CT) provides a promising approach in early lung cancer detection. Its high resolution characteristic allows researchers to count the blood vessels within tumors.

Although previous research has been conducted to explore efficient methods for early lung cancer detection, little progress is made. This is because early lung cancer is usually symptomless. It often progresses to an incurable stage before being detected. Lung cancer is the uncontrolled growth of abnormal cells in one or both lungs. These abnormal cells do not carry out the functions of normal lung cells and do not develop into healthy lung tissue. Cancer spreads by metastasis, the ability for cancer cells to penetrate into lymphatic and blood vessels, circulate through bloodstream, and then invade and grow in normal tissues elsewhere. Metastasis requires angiogenesis which is the formation of a network of new blood vessels. With angiogenesis, tumor growth proceeds [4]. It is known that tumor growth requires angiogenesis, but it is still unknown that whether there is a relationship between angiogenesis and the malignancy likelihood of pulmonary tumors.

Objective and Success Criteria
By taking advantage of CT’s high resolution characteristics, my project objective is to count the number of blood vessels within benign and malignant tumors and measure the nodule size (represented by radius, mm), thus determining whether there is a relationship between angiogenesis and the malignancy likelihood of pulmonary tumors. Based on Bagri et al. and Komen et al.’s research, the success criteria is that the malignant pulmonary tumors will exhibit more angiogenesis and will be larger as compared to benign pulmonary tumors[5].

METHODS
There are basically four steps. Firstly, lung CT scans were collected from totally 240 patients (n=240). 120 of the patients have malignant pulmonary tumors, which is also called lung cancer. The rest 120 patients have benign pulmonary tumors. Based on these samples, a single-blind experiment was conducted. All the samples were randomly rearranged before they were analyzed, so the investigator did not know whether the tumor was malignant or benign when he was analyzing it. Since a patient usually has more than one pulmonary nodule, only one pulmonary nodule was randomly picked for each patient. Then a Computer-Aided Diagnosis system was used to create a 3D model for the nodule. With this 3D model, the investigator was able to identify the nodule and visualize the lung blood vessels.

Next step was to measure parameters. The parameters needed to be measured for each nodule through 3D models include the nodule size and the number of blood vessels connected to each nodule. These two parameters for all 240 samples were manually measured. It usually took 15-30 minutes for each sample. There parameter were measured by another investigator for every 15 samples to check for experimental bias.

Finally, a 2-sample t-test was conducted based on the collected data from 240 samples. A statistical analysis was performed using ANOVA based on the average number of blood vessels and the average nodule size represented by radius (mm). The P-value was needed to be less than 0.05 to make the results significant.
RESULTS

Calculated values for average number of blood vessels connected to each nodule and nodule side (mm) based on 120 samples of malignant and benign nodules were shown in Figure 1 and Figure 2. P-value should be less than 0.0500 to make the results significant. Figure 1 compared the number of blood vessels between malignant and benign nodules. Malignant nodules had an average of 6.29 blood vessels with the standard error of 0.52, and benign nodules had an average of 4.93 blood vessels with the standard error of 0.34. The P-value=0.0380. The malignant nodules had more blood vessels connected than benign nodules. This meant that the malignant nodules showed more angiogenesis than benign nodules. Figure 2 compared the nodule size between malignant and benign nodules. The average size for malignant nodules was 8.01 mm with the standard error of 0.82, for benign nodules was 6.30 mm with the standard error of 0.45. The P-value=0.0320. The malignant nodules were significantly larger than benign nodules.

![Average number of blood vessels connected to one nodule](image)

**Figure 1:** Comparison of the number of blood vessels between malignant and benign nodules (P-Value=0.0380). The malignant nodule has more blood than benign nodule.

![Average size of a nodule](image)

**Figure 2:** Comparison of the nodule size (mm) between malignant and benign nodules (P-Value=0.0320). The malignant nodule is significantly larger than benign nodule.

DISCUSSION

The objective of the study was met. As compared to the success criteria, compared to benign pulmonary nodules, the malignant pulmonary nodules would exhibit more angiogenesis, which was consistent with the results, and would be larger, which was also the expected result. It was known that cancer spread by metastasis and metastasis required angiogenesis. So cancer spread was indirectly related to angiogenesis. The results showed that angiogenesis can imply the malignancy likelihood of pulmonary tumors.

Since lung cancer usually showed no symptoms in early stage, if this relationship could be detected in early stage, there would be higher probability to be diagnosed.

This study was limited by a few factors. The effects of gender, race, and age were not investigated in the study. These factors may probably affect the exact values that were calculated in results part. In addition, different cancer stages will also affect the survival probability. Stage is very important to prognosis – prediction of the cancer’s effect on the person who has it. On average, the higher the stage, the worse the cancer’s effect on the person who has it.

For future directions, a program that could allow the computer to count the blood vessels automatically instead of counting manually would significantly improve experiment efficiency. I also would like to investigate whether this kind of relationship can be applied to other cancers, such as breast cancer and prostate cancer.

CONCLUSION

Early lung cancer detection can improve the survival rate significantly. Lower-stage cancers generally have a better prognosis than higher-stage cancer. CT provides a promising approach in early lung cancer detection due to its high resolution characteristics. The nodule variable including the number of connected blood vessels and nodule size were investigated and analyzed. The results show that there is a relationship between angiogenesis and malignancy likelihood of pulmonary nodules, which can be applied in early lung cancer detection.

ACKNOWLEDGEMENTS

I would like to thank Dr. Jiantao Pu for his support for my study. I would also like to thank Mr. Suicheng Gu for his help in statistical analysis.

REFERENCES