Demonstration Application of invasive cryoablation for liver and lung cancer and standardization of its support technology—A prospective Multicenter study of combined cryoablation treatment system (Combined Cryosurgery System) for the liver and lung cancer: Efficacy and Safety

Background:
Cryoablation has been used in the treatment of various parenchymal tumors. The main mechanisms are as follows: At the centre of the cryoablative lesion is a sharply demarcated area of frozen necrosis where direct injury occurs. Cold-induced vascular injury causes damage to endothelial cells and cell junctions, which leads to platelet aggregation and microthrombosis. Apoptosis occurs in a peripheral zone of sublethal cold temperatures. Necrotic cells spill their extracellular contents, which can stimulate immune system.

Combined Cryosurgery System is a domestic high-tech invasive cryoablation system, which is invented by Chinese scientists and has independent intellectual property rights. Liquid nitrogen and absolute ethanol are used as refrigerant and heat working fluid respectively. The application of cold-heat alternation therapy can fully destroy the tumor cells. From 2013 to 2015, the RCT study on the safety and efficacy of Combined Cryosurgery System was conducted for patients aged 18-80 years with primary solid tumors (stage III-IV lung cancer, liver cancer and kidney cancer). The results showed that the effective rate of Combined Cryosurgery System was 97.6% after one month of cryoablation. The combined cryosurgery system produced safe and reliable effects with fewer probes, demonstrating its superior performance. Compared with similar foreign products, its advantages is obvious.

The purpose of this research are constructing a demonstration application center and promoting the clinical use of our domestic product (Combined Cryosurgery System) in the treatment of liver and lung tumors. For the patients diagnosed as typical liver and lung cancers, we have performed the combined cryoablation treatment in the clinical application and established the corresponding equipment configurations, clinical practice guidelines and service models. With the efforts of our clinical application and promotion, we believe that it is helpful to increase the market share of domestic medical devices.

Main purpose:
• To summarize the process of combined cryoablation treatment for liver and lung cancer and develop practice guidelines.
• To identify the efficacy and safety of the treatment and to provide objective data for the cryoablation treatment in liver and lung cancer.

Liver, lung cancer patients

<table>
<thead>
<tr>
<th>Treatment Procedure</th>
<th>Inclusion criteria</th>
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<tbody>
<tr>
<td>Liver cancer patients</td>
<td>Total: 188 cases</td>
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Positioning: CT guidance
Combined Cryoablation:
- Freezing lasts for 10-15 min, active thawing lasts for 5min.
- Repeat the above steps if needed (Freezing-active thawing)
- Pull out the probe with the temperature of 70-80 °C
- Wrap the skin puncture site.

Evaluation
Main research endpoints:
Local efficacy after cryoablation (4-6 weeks after first/last cryoablation)
Secondary research endpoints:
1. The 3-month and 6-month local control rate after cryoablation
2. local recurrence rate
3. QOL
4. OS
5. PFS

The status of enrollment:
A total of 97 patients have already enrolled in the research, of whom 65 patients and 32 patients are diagnosed as liver and lung cancer respectively. 53 patients with liver cancer and 31 patients with lung cancer participated in the evaluation of 3-month response rate.

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response rate: 92.9%

response rate: 100%