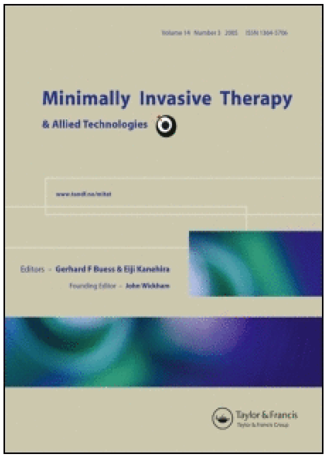

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ORIGINAL ARTICLE

Feasibility study on using an infrared thermometer for evaluation and administration of cryosurgery

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Abstract
Successful performance of cryosurgery relies heavily on a quick, efficient, safe and economic imaging way to monitor the surgical advancement and then to evaluate the curative effect. However, there is currently a lack of such an imaging modality. As for the commonly adopted imaging devices such as X-CT, MRI and PET, in addition their high cost and complexity in operation, they often induce additional scathe to the patients due to their potential radiation effects. Besides, in cryosurgery, the most important parameter – temperature – can not be directly detected by these methods. Considering the above factors, infrared thermography (IRT), a rather useful yet often neglected functional imaging technique in clinics, is proposed in this paper as an efficient tool for the quick evaluation and administration of a cryosurgical treatment of tumors. Based on skin surface temperature mapping, the degree of damage to the target tissue site caused by different freezing/heating protocols, as well as the states of blood circulation and metabolic heat generation within the treated region can possibly be identified. Further, through recording the temperature variation feature at the skin surface before and after cryosurgery, IRT would help to quickly evaluate the curative effect, which is very beneficial for later treatment planning. By detecting the surface infrared image and analyzing its digital values, the patient's invisible focus and abnormal physiological states, e.g. inflammations or pneumothorax, often accompanied by cryosurgical output yet difficult to determine via conventional imaging, could also possibly be diagnosed. To test the above concepts, both typical animal and clinical experiments were performed to demonstrate the feasibility and advantages of IRT-guided cryosurgery. This study may help push forward a novel, low-cost and non-contact way for an efficient performance of cryosurgery.

Key words: *Cryosurgery, imaging technique, medical infrared thermometer, surgery evaluation, clinical monitoring, minimally invasive therapy*

Introduction

With the rapid advancement of cryosurgery as a part of minimally invasive therapy, the imaging technique plays an increasingly important role (1–6) for a successful tumor treatment. In modern cryosurgery, the use of imaging for both monitoring and quantitative evaluation is often necessary. Up to now, the commonly adopted ways in cryosurgery have mainly relied on ultrasound (US), X-CT, magnetic resonance imaging (MRI) and positron emission tomography (PET) (7–15), some of which are gradually equipped with a temperature measurement function to meet the specific demands. Moreover, for a post-operational evaluation, in order to collect more information and guarantee a sufficient accuracy, hospitals even recommend the use of multiple image modalities, regardless of their cost. This leads to combined imaging systems such as fluorodeoxyglucose (FDG)-PET or PET-CT (16,17). However, due to their particularity and the complexity involved, the currently existing approaches do not seem sufficient to fulfill all clinical needs. Moreover, in real clinical situations, such imaging techniques are not the most efficient and cost-effective ones for patients with already advanced cancer, nor are they best suited for the evaluation of cryosurgical treatment output. This is because the effects of cryosurgery can not only be judged by the final casualty levels of the target

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tumor; there is also the possibility of the occurrence of harmful events such as freezing injury, inflammations, or pneumothorax. Considering these factors, IRT turns out to be a good alternative for the existing techniques since it can partially overcome the above barriers and serve as a potential assistant imaging technique for cryosurgery procedures.

The primary clinical areas for the use of an infrared system are the diagnosis of breast cancer and the identification of primary causes of undiagnosed pain. The first use of thermal diagnostics on humans could be traced back to 480 BC (8). In 1957, Lawson discovered that the skin temperature above a cancer in the breast is higher than that of normal tissue. In 1982, the FDA published its classification of thermography as an adjunctive, diagnostic screening procedure for the detection of breast cancer. With the fast development of this technique, infrared medical thermograph in health assessment has been quickly expanded (19,20), and it is now used for the diagnosis of disease or inflammation, burn evaluation and tumor hyperthermia monitoring. Several rather limited cases of applying infrared imaging (21–25) have also been reported in the field of cryobiology. However, few efforts have yet been made to apply such a method to systematically evaluate the curative effect of cryosurgery. We performed both animal and clinical tests to preliminarily demonstrate the potential value of implementing medical infrared thermometers for the evaluation and administration of cryosurgical treatment.

Principle

Infrared images record the thermal signatures of the desired skin area, and temperature patterns are displayed as either hyperthermic (hot) or hypothermic (cold). Normally, when finishing a cryosurgery procedure, not only the thermal property but also blood perfusion and the metabolic heat generation rate in the target tissues have changed due to freeze injury. Compared with the normal state before cryosurgery, such an irreversible procedure would generally result in a lowered temperature field at the skin surface. Using an infrared thermometer to continuously check such a phenomenon would thus provide valuable information complementary to that obtained by US, X-CT, and MRI. Moreover, with such an image processing system it is possible to obtain the average skin temperatures of certain specific regions as well as their distribution contrasts and trends. Such data is beneficial for a clinician to evaluate whether some diseased tissues still exist and then to estimate the therapeutic effectiveness. Furthermore, for the purpose of systematically evaluating the cryosurgery, a series of thermographs could be used to accurately reflect the whole cryosurgical procedure and to provide thermal information for an in-time planning of the following cryosurgical algorithms.

Animal tests and results

A commercially available medical infrared imaging system (HR-II, Institute of Optics and Electronics of North China, Beijing, China) was adopted to record the thermographs of the skin surface of a healthy rabbit before and after cryosurgery. To assure the accuracy of measurement, the device is calibrated by the manufacturer especially at low temperatures down to −40°C. Infrared thermographs were obtained at room temperatures around 23°C to 25°C. The relative humidity of the chamber was maintained at about 50% and air movement was limited to a minimum. The temperature resolution of the HR-II is ±0.1°C with a sensitivity of 0.05°C.

A healthy rabbit weighing about 2 kg was taken as the test object. Before the experiment, 10 ml 20%w ethyl carbamate was injected into the rabbit abdomen to induce general anesthesia. The rabbit was then fixed on an operating table. The outer side of the left thigh of the rabbit was chosen as the position for the cryosurgical operation and temperature mapping. To reduce its influence on the thermograph, the fur covering the surgical area was carefully shaved before cryosurgery. Figure 1 is a sketch of the experimental set-up, and Figure 2 shows the place where the cryoprobe is to be inserted. The combined freezing/heating system as described in (26) was used in this study. One cryoprobe with a diameter of 5 mm was percutaneously inserted into the thigh tissues at a depth of about 1cm. The temperature at

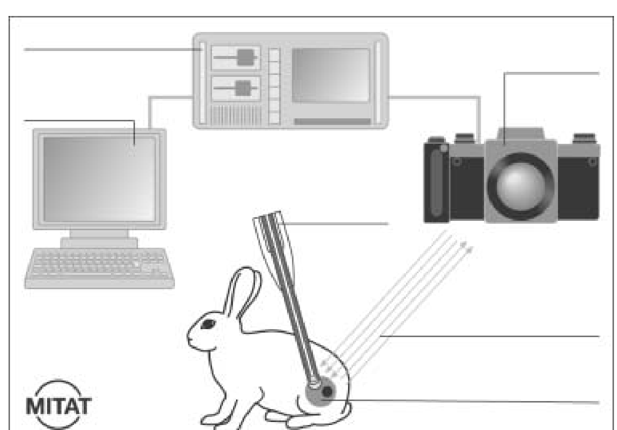


Figure 1. Sketch of the experimental set-up.

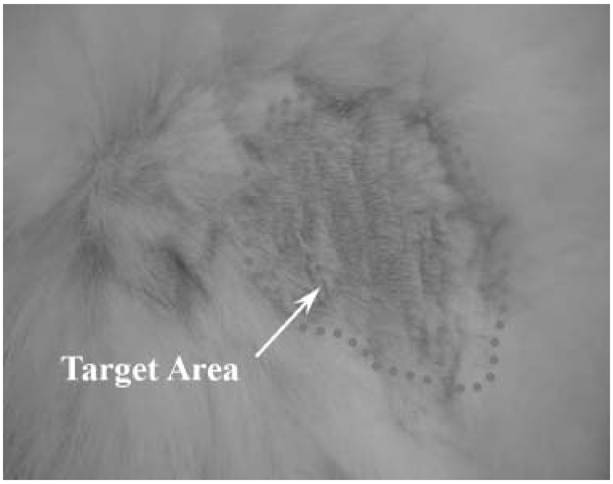


Figure 2. Appearance of the position at which the cryoprobe is to be inserted.

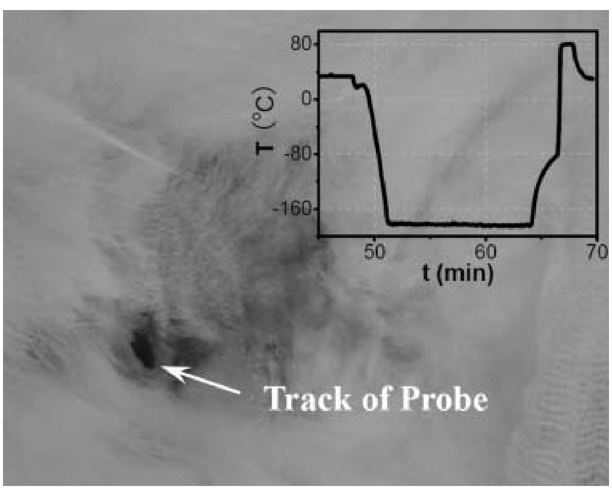


Figure 3. Appearance of the wound caused by the insertion of the cryoprobe and the temperature response of the probe during cryosurgery.

the tip of the cryoprobe was recorded by an embedded thermocouple. Figure 3 shows the wound caused by the insertion of the probe and the temperature response of the probe during cryosurgery. Figure 4 shows the thermographs of the skin surface above the target area, indicating the temperature mappings for the states measured before cryosurgery, 20 minutes after cryosurgery, and 24 hours after cryosurgery, respectively.

Clearly, infrared thermography has a good capability to quickly distinguish potential differences in a cutaneous temperature. Figure 4 (a) and (b) show that the temperature at the region covering the wound decreases dramatically. To better quantify the temperature variations, a poikilothermia region with an average diameter of 20 mm on the surface of the target is defined as a white circle as shown in Figure 4. Through the calculation of the average temperature at this defined region, it was found that the temperature dropped up to 20°C from the original temperature (35°C) to the final state (15°C). Such phenomena reflect to some extent certain correlations between the cutaneous conditions and the variations of physiological properties such as blood perfusion, metabolic heat generation and the freezing injury effect to the target tissues deep inside the biological body. Due to the rapid response of infrared thermographs, such temperature information can be gathered and analyzed and could then serve as the guideline for the final evaluation of the cryosurgical outcome. Furthermore, Figure 4 (b) shows that the minimum temperature around the probe track is still <10°C even after freezing has been stopped for 20 minutes. This shows that the treated area would possibly have been injured, which corresponds with the situation shown in Figure 3, where no thermal protection was administrated during cryosurgery. Therefore, using IRT makes it easy to monitor abnormal phenomena

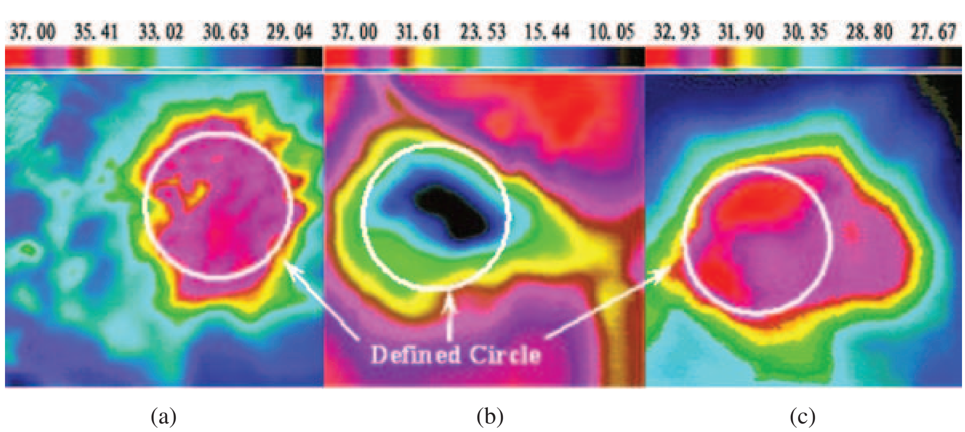


Figure 4. Thermographs on the skin surface above the target tissue area before and after cryosurgery (animal test); (a) before cryosurgery, (b) 20 min after cryosurgery, (c) 24 hours after cryosurgery.

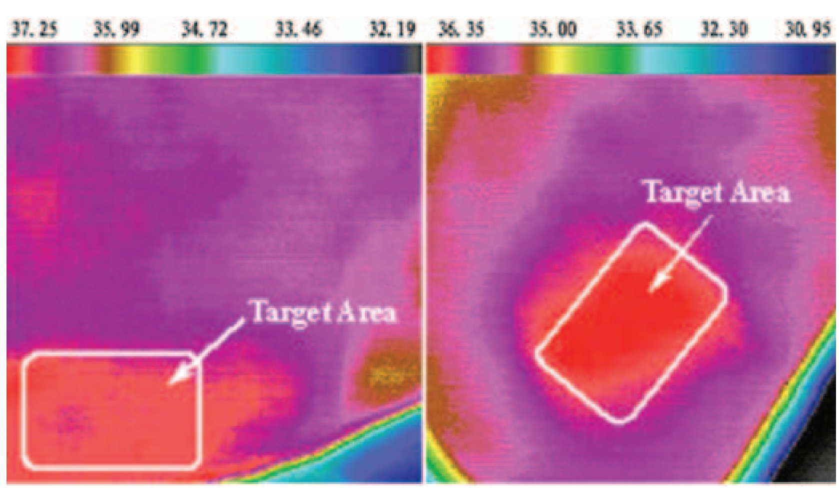
during cryosurgery and could offer potential valuable reference to assist conventional imaging inspections in quickly drawing a comprehensive conclusion regarding the cryosurgical output. Here, since there is no tumor inside the healthy rabbit thigh, the skin surface temperature distributes uniformly (Figure 4 a). After the cryosurgery, the thermographs in Figure 4 (b) and (c) indicate the cold and thermal spots, respectively, which represents the special temperature distribution trend. Such differences due to injury from cryosurgery could be sensitively detected by IRT and quickly displayed on the monitor. Thus clinicians could analyze, perform post data processing, and then plan for the following cryosurgical treatment.

The contrast between Figure 4 (a) and (c) proves what could have been expected to some extent. Even after 24 hours, the temperature at the same position still decreases by an average magnitude of 5°C. The maximum temperature decreases from 37°C to 32.9°C, which is mainly attributed to the treatment by cryosurgery. It could be speculated that the target area is traumatized to some extent, excluding the influence of skin frostbite and unmelted iceball. Besides, the temperature field reveals the non-uniformity in Figure 4 (c). Parts of the monitoring area appear to have an abnormally high temperature (thermal spot), which probably resulted from inflammation, emerging as scattering around the wound. Clearly, cryosurgery has caused an injury to the tissues of the healthy rabbit, which as a result induced inflammation at the wound. Such a phenomenon can easily be found and monitored when using thermographs. Considering such possible merits of using IRT for cryosurgery, future attention can be focused on how to establish a direct correlation between cutaneous temperature, frozen necrosis, and cell death. For such purposes, a series of thermographs and pathological tests in animal tests should be performed to establish standard algorithms to systematically quantify the killing scope of cryosurgical treatment.

Clinical test and results

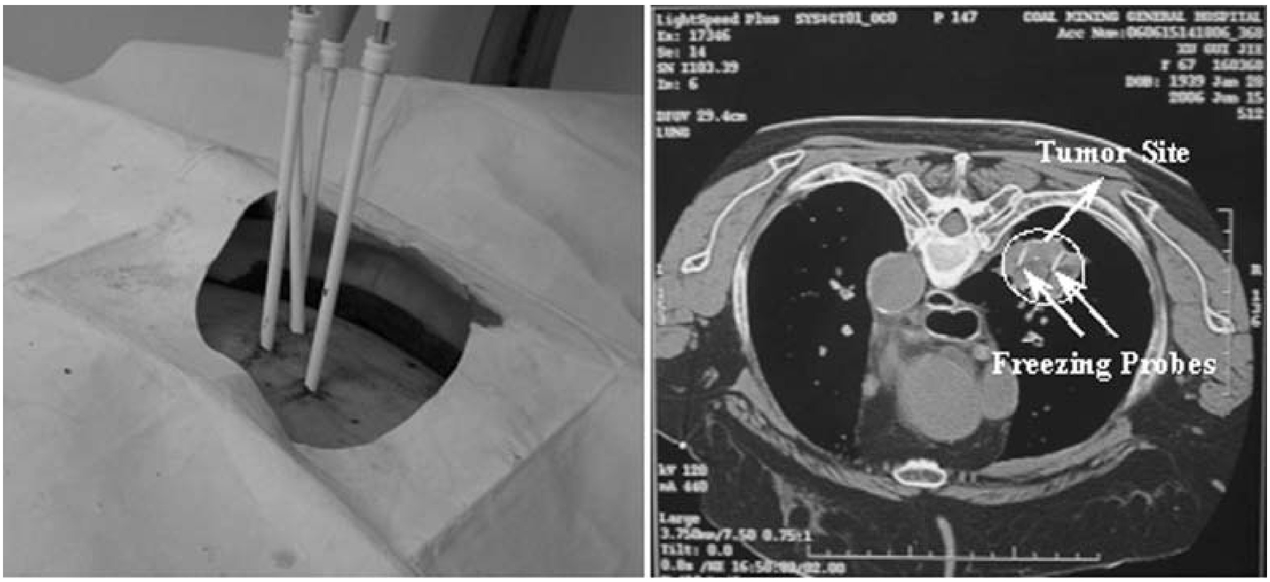
To further illustrate the feasibility and potential advantages of using infrared imaging systems for the evaluation of a real cryosurgical outcome, a series of temperature mapping on patients was also performed, along with the clinical treatment as routinely given at the General Hospital of Coal Industry Ministry of China, Beijing. Since the infrared imaging is completely non-contact, the temperature measurement process causes no disturbances to the surgery. All the experimental procedures and protocols were approved by the Clinical Committee of General Hospital of Coal Industry Ministry of China. Restricted by the limited number of patients tested, only some typical pictures are available and will be shown and discussed here. A white square in Figures 5 and 7 stands for the target tissue at the region of interest via contrast of optical and thermographic pictures.

Case1: Woman, aged 67, with a peripheral type carcinoma sized 6.6 cm x 5.2 cm at the right lung. The thermographs at the skin surface above the tumor were taken one day before and one day after cryosurgery. The corresponding results are shown in Figure 5. The cryosurgical operation was administrated by Ar-He cryoprobe system (Endocare Inc.,



(a) (b)

Figure 5. Infrared thermographs on skin surface above the target tissue area (a) one day before and (b) one day after cryosurgery for case 1.



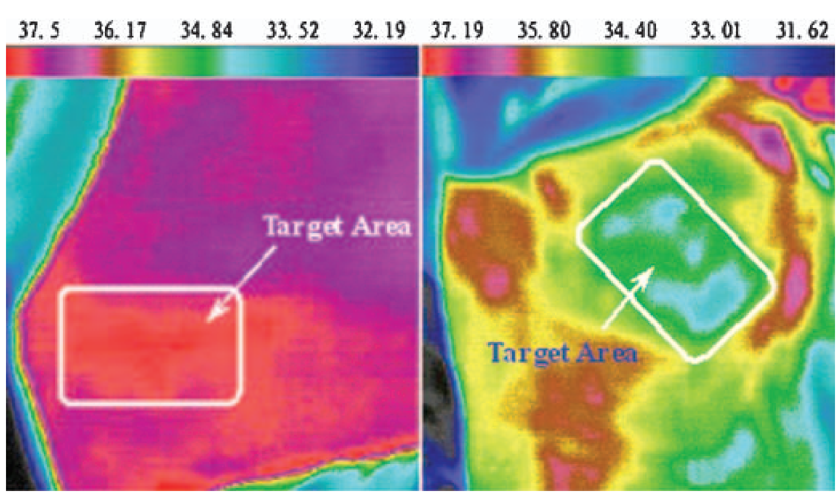
(a) (b)

Figure 6. Optical and CT pictures of the cryosurgical procedure for case 1; (a) cryosurgical incision, (b) intraoperative CT during cryosurgery.

Irvine, CA, USA), in which four cryoprobes were used. As a reference, the real cryosurgical incision setup and the picture of intra-operative CT during freezing are both shown in Figure 6 to illustrate the operational procedure and corresponding tumor information. The operation included two freeze-thaw cycles, and each cycle was composed of 10 min freezing and 5 min re-warming procedure. The infrared thermometer was focused on this area at an appropriately far distance beside the patient's bed.

A comparison of Figure 5 (a) and Figure 5 (b) shows that the average temperature at the target area is slightly decreased (about 1°C) one day after cryosurgery. This decreasing magnitude is very close to that of the animal test (about 3°C) shown in Figure 4 (a) and (c). Some possible causes for this slight difference may include the following:

- This patient has solid tumors deep inside the skin while the rabbit does not.
- The place of the focus is quite different, and so are the distributions of inner environment around the probes.
- The operational plan and cryosurgical procedure are also different. In addition, the patient's sweat around the wound area represents an interference and affects the surface temperature.



(a) (b)

Figure 7. Thermographs on the skin surface above the target tissue area (a) one day before and (b) one day after cryosurgery for case 2.

When using IRT for cryosurgery we find that the size and depth of tumors as well as the size of iceball are all factors which can affect the temperature profile at the skin surface. Therefore this could be a good opportunity to understand how the body's interior condition correlates with the evident changes of the surface temperature profile and its distributions.

Case 2: Man, aged 70, primary peripheral type carcinoma of the right lung with tumor size 8 cm × 12 cm. The thermographs at the skin surface above the tumor were taken one day before cryosurgery and 13 days after cryosurgery, respectively, and the results are given in Figure 7. Four cryoprobes were used in cryosurgery. The operation process included two freeze-thaw cycles with 10 min freezing and 5 min re-warming.

Figure 7 shows that the average temperature within the white circle decreases from 37°C to about 34°C. Moreover the distributions of temperatures appear non-uniform. Some cold spots were found to emerge scattering around the target places, which is quite different from both the previous case and the animal tests. Comparing Figure 4 (c), Figure 5 (b) and Figure 7 (b), the obvious contrasts were clearly revealed by IRT. Standard imaging analysis by a CT check found the treatment result of this patient to be very successful, which corresponds with the result provided by the thermometer. Here, the cold spots at the skin surface evidently reflect the thermal states at the target area where tumors are totally destroyed and the relevant vessels and metabolism at these tissue areas no longer contribute to the heat generation. In addition from the cutaneous temperature thermograph of the wound area, there are no freeze injuries or inflammations. This patient left the hospital soon after infrared test and CT check, which indicates that his cryosurgical treatment was very efficient. This result and the coherence of output fully prove the feasibility of using IRT for a quick evaluation on cryosurgery and treatment planning.

Discussion

Based on a series of comparisons of thermographs on the tested subjects taken before and after cryosurgery, it was demonstrated that it is feasible to quickly detect the effectiveness of curative outcomes using IRT; this may lead to the establishment of a straightforward and cost-effective way of managing freezing and rewarming procedures. Therefore if the image discloses an unfavorable operational result, it could remind cryosurgeons to improve their treatment plan in time to avoid failure of surgery, or reduce possibility of tumor spread and regeneration. Meanwhile with its repeatable and non-contact safe characteristics, the thermal image could be flexibly used to trace the development of patients' health condition after cryosurgery, which then serves as a valuable guidance for the following treatment. Clearly, this post-operational evaluation during recovery demonstrates that it is a potential tool in supplementing the conventional imaging check. Moreover by means of quick response to the surface temperature change, the IRT functional imaging technique will play an increasingly important role in detecting abnormal physiological phenomena induced by cryosurgery and will help clinicians to better evaluate the whole operation.

However, due to the complex mechanism of temperature responses at the target tissues and restricted by certain specific clinical situations, many factors should be carefully considered before pushing the present method into practice. For example, skin evaporation may affect the thermographic assessment. In addition, to quantify and establish a relevant algorithm amongst some important factors such as properties and features of tumors, the operational procedure and cutaneous information need to be further investigated. From our primary clinical experience, superficial tumors seem to produce better results than the deep ones when using IRT to monitor and evaluate the cryosurgery because the cutaneous temperature information reflects the real situation of tumors close to the skin much more precisely than that of the deeper ones. The degree of destruction of a solid tumor in the deep biological body is quite difficult to determine only by skin IRT. To further improve the evaluation accuracy, some digital graphic processing techniques should be developed in the near future to quantify the diagnostics. Further, along with some kind of mathematical simulation, the surface temperature information can easily be incorporated into the computer code to reconstruct the spatial and transient temperature field around the internal tumor object. The obtained data will serve as an important index for effectively improving the cryosurgery on the target tissues. It should be pointed out that, to make the medical infrared system more practical, additional clinical tests are still needed and more clinical experiences should be collected. At the same time a set of criteria for cryosurgical evaluation using IRT should be established to assure the measurement accuracy and its scope of application should be further clarified. All in all, the novel concept as proposed here is still at an early stage. Research efforts will be continued both in pathological evaluation and clinical tests.

Conclusion

Through a series of in vivo animal and clinical experiments it can be concluded that the implementation of IRT for a comprehensive evaluation on cryosurgery has potential advantages compared with conventional imaging techniques. Some of these benefits can be summarized as follows:

- IRT is repeatable, enabling many examinations in a non-contact way;
- the method is easy and convenient for operations, which warrants its widespread use in the near future;
- the imaging is flexible, less condition-limited, and real-time monitored;
- the IRT equipment is much cheaper than most conventional imaging systems;
- temperature mapping is a powerful and sensitive functional imaging technique which can quickly reflect variations of local blood flow and metabolism state and quickly detect diseased phenomena during cryosurgery.

Clearly, the temperature profile at the target area can show that before cryosurgery, a tumor has a relatively higher temperature than the surrounding area, which usually results in certain thermal spots and non-uniform temperature distributions at a position above the skin surface, and that after cryosurgery this temperature will be reduced slightly to a steady state which could be lower than that of the normal state. For a relatively successful cryosurgery, such cold spots often appear apparently above the wound area after a short recovery time, while for a failed cryosurgery such phenomena will not appear. If continuously taking thermographs spanning a long period such as from one day before cryosurgery to 1–2 weeks after cryosurgery, the accuracy of evaluation on the treatment can still be improved. Of course, the imaging process should be taken under the condition that the patient is in a natural state and room temperature and air remain relatively stable. Besides, artificial interference to IRT including sweating or inflammation should be reduced as much as possible. Further, if CT or other conventional imaging is also available, the infrared thermographs should be taken on the same day for comparative evaluation. All in all, some basic features of this new method have been successfully illustrated through animal and clinical tests and its further extension in cryosurgical clinics will be the next step in the following research.

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References

1. Exacoustos C, Zupi E, Marconi D, Romanini ME, et al. Ultrasound-assisted laparoscopic cryomyolysis: two- and three-dimensional findings before, during and after treatment. Ultrasound Obstet Gynecol. 2005;25:393–400.
2. Coldwell DM, Sewell PE. The expanding role of interventional radiology in the supportive care of the oncology patient: from diagnosis to therapy. Semin Oncol. 2005;32: 169–73.
3. Wagner AA, Solomon SB, Kavoussi LR. Imaging following cryoablation of a renal lesion. Nat Clin Pract Urol. 2005;2: 52–7.
4. Simon CJ, Dupuy DE. Current role of image-guided ablative therapies in lung cancer. Expert Rev Anticancer Ther. 2005;5:657–66.
5. Harada J, Mogami T. Minimally invasive therapy under image guidance–emphasizing MRI-guided cryotherapy. Rinsho Byori. 2004;52:145–51.
6. Regoly-Merei J. Current diagnostics and therapy of focal liver lesions Orv Hetil., 2003;144:2299–309.
7. Tacke J, Speetzen R, Heschel I, Hunter DW, et al. Imaging of interstitial cryotherapy–an in vitro comparison of ultrasound, computed tomography, and magnetic resonance imaging. Cryobiology. 1999;38:250–9.
8. Donnelly BJ, Saliken JC, Ernst DS, Weber B, et al. Role of transrectal ultrasound guided salvage cryosurgery for recurrent prostate carcinoma after radiotherapy. Prostate Cancer Prostatic Dis. 2005;8:235–42.
9. Zhu Q, Shimizu T, Endo H, Kodama Y, et al. Assessment of renal cell carcinoma after cryoablation using contrast-enhanced gray-scale ultrasound: a case series. Clin Imaging. 2005;29:102–8.
10. Gupta A, Allaf ME, Kavoussi LR, Jarrett TW, et al. Computerized tomography guided percutaneous renal cryoablation with the patient under conscious sedation: initial clinical experience. J Urol. 2006;175:447–53.
11. Warlick CA, Lima GC, Allaf ME, Varkarakis I, et al. Clinical sequelae of radiographic iceball involvement of collecting system during computed tomography-guided percutaneous renal tumor cryoablation. Urology. 2006;67:918–22.
12. Kodama Y, Abo D, Sakuhara Y, Sawada A, et al. MR-guided percutaneous cryoablation for bilateral multiple renal cell carcinomas. Radiat Med. 2005;23:303–7.
13. Zhu Q, Shimizu T, Abo D, Jin M, et al. Magnetic resonance imaging findings and histopathological observations after percutaneous renal cryoablation in the rabbit model. J Urol. 2006;175:318–26.
14. Zu C. Evaluation of MRI findings and histopathological changes in the rabbit kidney following transcutaneous cryogenic surgery. Hokkaido Igaku Zasshi. 2005;80: 279–87.
15. Bolte SL, Ankem MK, Moon TD, Hedican SP, et al. Magnetic resonance imaging findings after laparoscopic renal cryoablation. Urology. 2006;67:485–9.
16. Nishiyama Y, Yamamoto Y, Yokoe K, Monden T, et al. Contribution of whole body FDG-PET to the detection of distant metastasis in pancreatic cancer. Annals of Nuclear Medicine. 2005;19:491–7.

17. Jager PL, Slart R, Corstens FHM, Hoekstra OS, et al. PET-CT: a matter of opinion? European Journal of Nuclear Medicine and Molecular Imaging. 2003;30:470–1.
18. http://www.american-medical-infrared-academy.com/medicalinfrared.html.
19. Liddington MI, Shakespeare PG. Timing of the thermographic assessment of burns. Burns. 1996;22:26–8.
20. Ogan K, Roberts WW, Wilhelm DM, Bonnell L, et al. Infrared thermography and thermocouple mapping of radiofrequency renal ablation to assess treatment adequacy and ablation margins. Urology. 2003;62:146–51.
21. Choi B, Welch AJ. Infrared imaging of 2-D temperature distribution during cryogen sprays cooling. J Biomech Eng. 2002;124:669–75.
22. Pogrel MA, Yen CK, Taylor R. A study of infrared thermographic assessment of liquid nitrogen cryotherapy. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 1996;81:396–401.
23. Junila J, Kaarela O, Makarainen H, Waris T. Assessment of tissue viability by thermography after experimentally produced frostbite of the rabbit ear. Acta Radiol. 1993;34:622–4.
24. Palmer CM, Siebke K, Yeates DK. Infrared video thermography: a technique for assessing cold adaptation in insects. Biotechniques. 2004;37:212–4, 216–7.
25. Rich PB, Dulabon GR, Douillet CD, Listwa TM, et al. Infrared thermography: a rapid, portable, and accurate technique to detect experimental pneumothorax. J Surg Res. 2004;120:163–70.
26. Liu J, Zhou YX, Yu TH, Gui L, et al. Minimally invasive probe system capable of performing both cryosurgery and hyperthermia treatment on target tumor in deep tissues. Min Invas Ther and Allied Technol. 2004;13:47–57.