Effective necrosis of tumor using multihole nozzle in cryospray

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by

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CHAPTER 7

Conclusions

There are four sections in the thesis. The first three sections deal with the experiments conducted to establish the role of multihole nozzle in cryoablation. The three parts are arranged in the following order: (i) Characterization of performance of multihole nozzle in cryospray followed by optimizing its different parameters for cryospray process, (ii) Establishing relation between in-vivo and in-vitro cryospray experiments through thermal characteristics, and (iii) Experimental study to characterise the role of multihole nozzle in adjuvant assisted cryospray. The last section is a numerical study in which Eulerian-Lagrangian model is developed to simulate the interaction of liquid nitrogen spray with the surrounding and its effect on cryablation is quantified.

A distinctive trend is always observed in the geometry of skin cancer, i.e. more lateral spread on superficial skin as compared to the penetration depth into the skin. It means more cooling is required in radial direction as compared to that in the axial direction. SHN used in current scenario fails to provide the desired effect. Therefore, the main aim of the study is to develop a prototype of a multihole nozzle that can eradicate the existing limitations of current cryospray process. In this regard, chapter 3 presents the influence of several parameters of MHN like number of holes, pattern of hole, margin among the holes and spraying distance on cryoablation. These parameters are quantified through in-vitro experiments. The cryoablation on the surface of the phantom is ascertained through thermal images whereas the cryoablation below the surface of the phantom is ascertained through thermocouples. It has been observed that area of cryoablation on the surface of phantom with MHN is twice larger than the area of cryoablation with SHN. The ratio of lateral spread to the penetration depth of ice ball is found to be almost same for SHN and MHN. It means MHNs provide more cryoablation in the lateral direction as compared to that in the axial direction. After acknowledging the role of MHN in cryoablation, six MHNs with difference in number of holes and margin are fabricated to establish the role of these parameters in cryoablation. The MHNs with central hole is found to be dominant in terms of cryoablation than MHNs without the central hole. The enhanced mass flow rate and reduced evaporation during the flight of cryogen from nozzle exit to phantom surface are the reason for this. The desired cooling rate of 50 ^{0}C/min to 200 ^{0}C/min is obtained upto a depth of 2 mm below the gel surface and in a radius of 10 mm from the centre of spray with five MHNs among the six MHNs selected in the study. However, SHN failed to provide desired cooling rate upto aforementioned locations.

The in-vivo study of cryoablation conducted on healthy male rats established that biological factors like metabolic heat generation and blood perfusion are less dominant in cryospray because it deals with superficial lesions. Hence, results of in-vitro experiments can be replicated to in-vivo conditions. On the basis of histopathological results it can be observed that the necrotic zone of in-vitro experiment is smaller than the necrotic zone of in-vivo experiment. Natural thawing in in-vivo conditions is responsible for such observation because necrosis due to thawing is not acknowledged in the in-vitro experiments. The cryoablation achieved through MHN in in-vivo experiment is twice larger than that in SHN on the surface of gel.

Apart from modification of the equipment to increase the necrotic zone, adjuvant assisted cryospray with SHN is also explored in the present work. Nanoparticles are chosen as the adjuvants in the study. The characterization results advocate that the nanoparticles used in the study fulfill the size criterion of adjuvants administration in the skin. Among the three nanoparticles selected in the study, it has been observed that Magnesium Oxide nanoparticles register maximum cryoablation followed by Aluminum Oxide and Iron Oxide nanoparticles. The presence of these adjuvants in the phantom assists in achieving the desired combination of cooling rate and lethal temperature required for cryoablation through intracellular ice formation. As far as conventional cryospray technique (cryoablation with SHN without the presence of adjuvants in phantom) is concerned, the necrotic zone upto a surface area of 3.14 cm^2 with a penetration depth of 2 mm can be treated after 120 s of spray. Whereas, the present approach can treat lesion upto a surface of area of 7.5 cm^2 with a penetration depth of 2 mm.

Another study is conducted to explore the role of various parameters of MHN in adjuvant assisted cryospray. The maximum increment in cryoablation is achieved through MHN 5B (5 holes with 1.5 mm margin) on the surface of gel. The diameter of necrotic zone is 21 mm larger than that in the conventional approach (in normal-phantom with SHN) after 120 s of spray for the same spraying distance with MHN 5B. Moreover, the diameter of necrotic zone with MHN 5B is 11 mm larger than the diameter of necrotic zone with SHN in presence of adjuvant after 120 s of spray for same spraying distance.

The numerical study suggests that with increase in the spraying distance the dimension of radial ice ball increases and axial ice ball decreases. The jet disintegration increases with increase in the spraying distance. A spraying distance of 18 mm provides the most optimised results in terms of cryoablation for SHN of diameter 0.8 mm. It has also been observed that the temperature variation along the spray axis increases with increase in the spraying distance.

7.1 Scope for future study

It has been observed through the studies conducted so far in the field of cryospray that it is an effective cancer treatment modality. In order to establish cryospray as a routine skin cancer treatment method following aspects of cryospray should be addressed:

- The anatomy of human body changes with age, gender and orientation. Therefore, tissue phantoms which acknowledge the effect of bone and vascular network should be made to understand the physics of cryoablation that depends on the anatomy of body.

- The isotherms obtained through cryospray depend on the geometry of the lesion. Thus, the MHNs used in the study should be tested on nodular phantoms to estimate the propagation of lethal front in an asymmetric lesion.

- Our skin consists of three layers with different thermophysical properties and the thickness of skin depends on the part of the body. Therefore, more sophisticated phantoms comprising of different layers of skin can be developed to mimic the actual condition.

- Numerical modeling of heat and mass transfer inside the cryogun could provide a better understanding of flashing phenomenon in cryogen and elucidate the role of drop dynamics in cryoablation.

- Experiments should be conducted to examine the role of drop dynamics in liquid nitrogen spray. They are required to predict its heat and mass interaction with the tissue and the surrounding. These experiments will optimise its various parameters like sauter mean diameter, droplet velocity, heat transfer coefficient etcetra. The data obtained through these experiments will be helpful in the validation of numerical model.

- Administration of adjuvant inside the skin through transdermal route requires optimization of its various aspects like concentration of drug, duration of drug administration, mode of drug administration etcetra. Hence, experimental and numerical models can be developed to analyse each aspect of transdermal drug delivery.