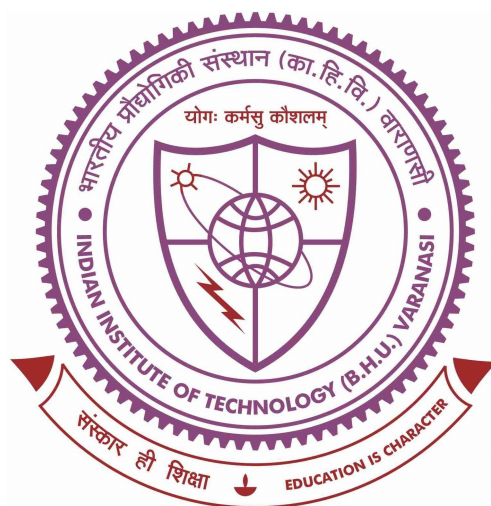


Effective necrosis of tumor using multihole nozzle in cryospray



*Thesis submitted in partial fulfillment
of the requirements for the degree of*
Doctor of Philosophy

by

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Contents

Certificate	i
Supervisors' certificate	iii
Declaration by the candidate	v
Copyright transfer certificate	vii
Acknowledgements	ix
Table of Contents	x
Abstract	xxi
1 Introduction	1
1.1 History of cryotherapy	1
1.1.1 Terminologies of cryotherapy	3
1.1.2 Diversity in cryotherapy	6
1.1.3 Modern Cryotherapy	8
1.1.4 Pros and cons of cryotherapy	11
1.1.4.1 Pros	11
1.1.4.2 Cons	12
1.1.5 Thesis structure	12
2 Literature Review	13
2.1 Spray characteristics of cryogen	13
2.2 Influence of equipment modification on cryoablation	19
2.3 In-vivo experiments in cryotherapy	20
2.4 Numerical modeling of cryoablation	22
2.5 Role of adjuvant in cryoablation	25

3	Characterization of performance of multihole nozzle in cryospray and optimization of its spray parameter	28
3.1	Materials and Method	29
3.2	Results and discussions	31
3.2.1	Uncertainty Analysis	32
3.2.2	Validation of thermal images	33
3.2.3	Comparison of cryoablation between SHN and MHN	35
3.2.3.1	Axial temperature distribution	36
3.2.3.2	Movement of axial ice front	40
3.2.3.3	Radial temperature distribution	41
3.2.4	Comparison among MHNs	45
3.2.4.1	Axial temperature distribution	45
3.2.4.2	Cooling rate	49
3.2.4.3	Radial temperature distribution	50
3.2.4.4	Conclusion	51
4	Establishing relation between in-vivo and in-vitro Cryospray experiments through thermal characteristics	53
4.1	Materials and Method	54
4.2	Results and discussions	56
4.2.1	Radial temperature distribution	56
4.2.2	Axial temperature distribution	59
4.2.3	Histology	60
4.3	Conclusion	62
5	Nano-cryospray: Thermal effect of adjuvants on cryoablation	63
5.1	Materials and Method	64
5.2	Characterisation of nanofluid	65
5.3	Uncertainty Analysis	71
5.4	Results and discussion	72
5.4.1	Influence of adjuvant on cryoablation with SHN	72
5.4.1.1	Axial Temperature Distribution	72
5.4.1.2	Radial temperature distribution	73
5.4.2	Influence of adjuvant on cryoablation with MHN	76
5.4.2.1	Axial Temperature Distribution	77
5.4.2.2	Radial temperature distribution	81
5.5	Conclusion	82

6	Numerical study on the spray and thermal characteristics of cryospray process	83
6.1	Mathematical model and numerical approach	83
6.1.1	Governing equations	84
6.1.1.1	Continuous phase (air)	84
6.1.1.2	Discrete phase (liquid nitrogen droplets)	86
6.1.1.3	Phase change in gel phantom	87
6.1.2	Boundary condition and operating parameters	88
6.1.3	Numerical approach and grid distribution	91
6.1.4	Grid independence and time independence	92
6.1.5	Code validation	93
6.2	Results and discussion	94
6.2.1	Temperature variation	94
6.2.2	Lethal front propagation	99
6.2.3	Freezing front propagation	102
6.3	Conclusion	102
7	Conclusions	106
7.1	Scope for future study	108
	Bibliography	111
	Author's Personal Profile and Publication List	129
	addcontentslinetocsectionList of Figures	

List of Figures

1.1	Influence of cooling rate on cell death [41]	4
1.2	Influence of lethal temperature and cooling rate on cell death [41]	5
1.3	Intracellular and Extracellular Ice Formation	5
1.4	Cryogun	6
1.5	Method of cryotherapy for superficial lesions	8
1.6	Various spray methods [170]	9
1.7	Overlapping spray technique [170]	10
1.8	Neoprene cones and cryoplates [170]	10
1.9	The schematic representation of cryospray	11
2.1	Pressure-volume curve for a fluid [20]	14
3.1	Experimental Setup	30
3.2	Positions of thermocouple	31
3.3	Transient temperature curves of thermocouples placed at 2 mm and 5 mm below the gel surface and 0 mm away from CS with 95% confidence interval for $z=18$ mm (MHN: Multihole nozzle, SHN: Singlehole nozzle, z : Spraying distance)	33
3.4	Transient temperature curves of thermocouples placed at 2 mm below the gel surface with 95% confidence interval for nozzle 4A, 4C, 5A, and 5C	34
3.5	Customised Nozzle	35
3.6	Commercial nozzle	36

3.7	Transient temperature curves of thermocouples placed at 2 mm below the gel surface and at different radial locations (MHN: Multihole nozzle, SHN: Singlehole nozzle z: spraying distance)	37
3.8	Transient temperature curves of thermocouples placed at 5 mm below the gel surface and at different radial locations (MHN: Multihole nozzle, SHN: Singlehole nozzle z: spraying distance)	38
3.9	Propagation of ice front for spraying distance (z)=18 mm	40
3.10	Thermal Images after 120 s of spray	41
3.11	Temperature distribution along the gel surface (MHN: Multihole nozzle, SHN: Singlehole nozzle, z: Spraying distance)	43
3.12	Movement of lethal and freezing front on gel surface (MHN: Multihole nozzle, SHN: Singlehole nozzle, z: Spraying distance, LF: Lethal front, FF: Freezing front)	44
3.13	Transient temperature curves of thermocouples placed at 2 mm below the gel surface and at different radial locations	46
3.14	Transient temperature curves of thermocouples placed at 5 mm below the gel surface and at different radial locations	48
4.1	Experimental Setup	54
4.2	Positions of thermocouple	55
4.3	Thermal images of in-vivo experiments with SHN	56
4.4	Thermal images in-vitro experiments with SHN	56
4.5	Thermal images of in-vivo experiments with MHN	57
4.6	Thermal images of in-vitro experiments with MHN	57
4.7	Temperature distribution along the surface	58
4.8	Transient temperatures at different locations	59
4.9	Histology results	61
5.1	Phantom used in the study	65
5.2	Characterisation of MgO nanoparticles	67
5.3	Characterisation of Al ₂ O ₃ nanoparticles	68
5.4	Characterisation of Fe ₃ O ₄ nanoparticles	69
5.5	XRD Pattern of nanoparticles	70
5.6	Transient temperature curves of thermocouples placed at 2 mm below the gel surface and 0 mm away (TC200 location) from CS with 95% confidence interval for different nano-phantoms	71

5.7	Transient temperature curves of thermocouples placed at 2 mm below the gel surface and at different radial locations for different phantoms	74
5.8	Transient temperature curves of thermocouples placed at 5 mm below the gel surface and at different radial locations for different phantoms	75
5.9	Thermal image of Al ₂ O ₃ nano-phantom after 120 s of spray	76
5.10	Transient temperature curves of thermocouples placed at 2 mm below the gel surface and at different radial locations	78
5.11	Transient temperature curves of thermocouples placed at 5 mm below the gel surface and at different radial locations	79
6.1	Actual Cryospray Process	84
6.2	Computational Doamin	85
6.3	Mass flow rate	89
6.4	Grid distribution for computational domain	91
6.5	Grid indenpence test	92
6.6	Code Validation	93
6.7	Comparison of spray image with the temperature contour of spray domain for z = 9 mm after 60 s	95
6.8	Comparison of spray image with the temperature contour of spray domain for z = 18 mm after 60 s	95
6.9	Comparison of spray image with the temperature contour of spray domain for z = 27 mm after 60 s	96
6.10	Centreline temperature distribution in the spray domain after 60 s of spray .	97
6.11	Transient temperature of a point on the tissue surface at a distance of 0 mm from the centre of spray (TC000 location)	98
6.12	Transient temperature of a point on the tissue surface at a distance of 5 mm from the centre of spray (TC005 location)	98
6.13	Transient temperature of a point on the tissue surface at a distance of 10 mm from the centre of spray (TC010 location)	99
6.14	Lethal front after 20 s	100
6.15	Lethal front after 40 s	100
6.16	Lethal front after 60 s	101
6.17	Transient temperature distribution across the tissue domain	103
6.18	Ice front after 20 s	104
6.19	Ice front after 40 s	104
6.20	Ice front after 60 s	105

addcontentslinetocsectionList of Tables

List of Tables

1.1	Cooling agents used by researchers [170]	2
1.2	Properties of liquid nitrogen	3
1.3	Diversity in cryotherapy	6
2.1	Studies on flash evaporation	15
2.2	Applications of flashing in Cryotherapy	17
2.3	Numerical studies on cryoablation	23
3.1	Nozzle Geometry	29
3.2	Verification of data generated through FLIR Camera	34
3.3	Cooling Rate ($^{\circ}\text{C}/\text{min}$) for various thermocouples for a spraying distance of (z) = 18 mm	40
3.4	CR ($^{\circ}\text{C}/\text{min}$) for various thermocouples for various MHNs	49
3.5	Movement of lethal front and freezing front (in mm) on the gel surface with respect to time	50
5.1	Cooling Rate ($^{\circ}\text{C}/\text{min}$) of nano-phantom and normal-phantom for a spray- ing distance of (z) = 18 mm	73
5.2	Movement of lethal front and freezing front (in mm) on the gel surface with respect to time	75
5.3	Difference in end temperature of nano-phantom and normal phantom [155]	77
5.4	Cooling rate ($^{\circ}\text{C}/\text{min}$) of nano-phantom and normal phantom [155]	81
5.5	Movement of lethal front and freezing front (in mm) on the gel surface after 120 s of spray	81

List of Symbols and Abbreviations

u	velocity (m/s)
t	time (s)
p	pressure (Pa)
g	gravitational acceleration (m/s ²)
T	temperature (K)
D_Y	mass diffusion coefficient of vapor (m ² /s)
h	enthalpy (J/kg)
Y	mass fraction of vapor
S	Source term
m	droplet mass (kg)
c_p	specific heat (J/kg.K)
h_c	convective heat transfer coefficient (W/m ² K)
A	droplet surface area (m ²)
L_h	latent heat of water vaporization (J/kg)
d_d	droplet diameter (μ m)
B_T	thermal Spalding number
Re	Reynolds number
Pr	Prandtl number
F_D	drag force (N)
F_d	force exerted on droplet (N)

Greek symbols

ρ	density (kg/m ³)
μ	dynamic viscosity (Pa.s)
λ	thermal conductivity (W/mK)

Subscript

g	mixture gas
d	droplet

Acronym and other notations

MHN	Multihole nozzle
SHN	Singlehole nozzle
CS	Centre of spray

z	Spraying distance
CR	Cooling rate

Abstract

Cryospray is a process in which liquid nitrogen is sprayed on a superficial cancerous lesion to achieve necrosis. In order to achieve necrosis through cryospray a combination of particular cooling rate and lethal temperature is required. The small aperture of single hole nozzle (SHN) and less mass flow rate associated with it reduce the rate of heat transfer from the lesion. Moreover, the low thermal conductivity of lesion further reduces the rate of energy diffusion inside it. These limitations associated with the existing method of cryospray fail to provide complete necrosis in the lesions larger than 15 mm in diameter.

Moreover, 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. Cryospray techniques followed in current scenario compels surgeons to use single hole nozzle to treat skin cancer. The SHN provides less lateral spread compared to penetration depth, which ultimately lingers the process and the chances of healthy tissue destruction also increase due to over penetration of cryogen. In this perspective, six multihole nozzles (MHN) are designed and fabricated to study their influence on cryoablation. It has been observed through in-vitro study that these customised MHNs can rule out the existing limitations of cryospray. The designed MHNs are capable enough to treat larger lesions in terms of lateral spread in one sitting as compared to the existing methods that require more than one sitting, resulting in a fair amount of discomfort to patients. Several governing factors of cryoablation like spraying distance, number of holes in the nozzle, margin among the holes and spray duration are optimised for the MHN. The optimum range of cooling rate and lethal temperature required for the intracellular ice formation is obtained upto 15 mm from the centre of spray (on the surface of gel) when MHNs are employed to spray cryogen. However, commercial SHN fails to provide such outcomes.

These nozzles (MHNs) are tested under the in-vivo conditions as well. An in-vivo experiment is performed on healthy male rats (Charles Foster rats) weighing about 150–200 g while the in-vitro experiment is performed on tissue phantom. Single freeze–thaw cycle (freezing 120 s and thawing 130 s) with a spraying distance of 18 mm is selected for both the experiments. A comparative study between customised MHN (with 5 holes and margin 2 mm) and commercial SHN is conducted to analyze the impact of number of holes on cryoablation in in-vivo conditions. It is an attempt to explore the difference between in-vivo and in-vitro experiments. The data extracted through thermocouples advocates that biological factors have negligible impact on cryoablation. However, histopathological results suggest that in-vivo necrotic zone is larger than the in-vitro necrotic zone; natural thawing is responsible for such behavior. The area of cryoablation on the surface of rat skin is 50 % larger when cryogen is sprayed through MHN as compared to SHN.

As mentioned above, a combination of particular cooling rate and lethal temperature is required to achieve necrosis through cryospray. MHNs used in the study fulfill that requirement upto a depth of 2 mm below the gel surface and in a radius of 10 mm from the centre of spray when the spraying distance is taken as 18 mm and the duration of spray is kept constant as 120 s for all the cases. The dimensions of necrotic zone for the same spray duration and the spraying distance can further be improved with the introduction of adjuvant in the lesion. Thus, in-vitro experiment to quantify the role of adjuvant in cryoablation with MHNs is also carried out in the study. A comparative study between nano-phantom and normal-phantom is conducted to examine the influence of adjuvant in cryoablation. The most promising adjuvant and MHN for efficient cryoablation are obtained through the study. It is found that Magnesium Oxide nanoparticle provides the most optimised result with MHN having 5 holes and margin 1.5 mm in terms of cryoablation. The proposed approach is employed with SHN as well. It has been observed that lesions with a surface area of 7.5 cm^2 and a penetration depth of 2 mm can easily be treated through the administration of MgO nanoparticles with SHN. On contrary, conventional technique of cryospray (without administration of adjuvant) can treat lesions with a surface area less than 3.14 cm^2 with a penetration depth of 2 mm.

The amount of cooling produced by cryogen during the spray depends on its interaction with the surrounding. Cryogen sprays are different from liquid sprays in which mechanical forces cause the atomisation of liquid. The saturation temperature of cryogen is much lower than the ambient temperature, therefore flashing occurs in the cryogen as they interact with the surrounding. Flashing causes primary atomisation of the droplets. Also, secondary break up occurs due to the surface tension of the droplets and velocity difference between the two phases. Thus, during its (cryogen) flight from nozzle exit to the cooling surface, cryogen exchanges heat and mass with the surrounding. The experimental and numerical studies conducted so far in the field of laser dermatology have enhanced the understanding of this phenomenon but absorbing its full potential in cryospray requires more research. In this perspective, an Eulerian- Lagrangian mathematical model is developed to simulate the behavior of cryogen spray. The effect of spraying distance on necrosis is quantified. The multi-phase flow of cryogen emanating from commercial cryospray nozzle is validated against the experimental result. The axial depth and radial spread of ice ball are found to increase by 15 % and 25 % respectively when the spraying distance is changed from 27 mm to 9 mm. It is also noticed that spray dispersion increases with the duration of spray. It causes a larger necrotic zone in radial direction than that in the axial direction with respect to time. It has been observed that the spraying distance of 18 mm is providing the most optimised necrotic zone among the three spraying distances

considered in the study.

***Keywords:* Thermal Imaging Camera; Cryospray; Multihole nozzle; Singlehole nozzle; Necrotic zone; Nanoparticle; Flashing;**

