

Canady Helios Cold Plasma Dosimetry to Treat Solid Tumors

Olivia Jones¹, Xiaoqian Cheng, Ph.D.¹, Saravana R.K. Murthy, Ph.D.¹, Lawan Ly¹, Annisa Elbedour¹, Taisen Zhuang, Ph.D.¹, Aviram Nissan, M.D.², Steven Gitelis, M.D.³, Mohammad Adileh, M.D.², Alan Blank, M.D.³, Matthew Colman, M.D.³, Cristina O'Donoghue, M.D.³, Kerstin Stenson, M.D.³, Karen O'Hara³, Michael Keidar, Ph.D.⁴, Giacomo Basadonna, M.D. Ph.D.⁵, and Jerome Canady, M.D.^{1,4,6*}



¹Jerome Canady Research Institute for Advanced Biological and Technological Sciences, Takoma Park, MD, USA

²Sheba Medical Center, Tel HaShomer, ISRAEL

³Rush University Medical Center, Chicago, IL, USA

⁴The George Washington University, Washington DC, USA

⁵University of Massachusetts School of Medicine, Worcester, MA, USA

⁶Holy Cross Hospital, Silver Spring, MD, USA

* Correspondence: drjcanady@jcric-abts.com; Tel.: +1-(301)270-0147

Introduction

Cold atmospheric plasma (CAP) technology has emerged as a unique and selective cancer treatment with great potential to advance the field of surgery. A variety of CAP devices have demonstrated anti-cancer capabilities on cell lines and patient derived tissues. The next frontier is the use of CAP to directly treat cancer in humans. Existing challenges in cancer treatment include toxicity, tumor recurrence, and diverse pathologies among solid tumors. These factors make it difficult to apply new treatments to multiple types of cancer. CAP is uniquely positioned to address this because of its low toxicity and acute selectivity.

CAP has effectively killed solid tumor cell lines including, breast, brain, bile duct, and pancreatic cancers in a dose dependent manner [1, 2]. Most of this research provides insights on CAP selectivity for specific cancers; however, fewer studies provide data on a wide range of solid tumors at one time. Canady Helios Cold Plasma (CHCP) has been demonstrated to effectively eliminate solid tumors including renal, colorectal, ovarian, pancreatic, esophageal and breast adenocarcinoma without thermally damaging normal tissue [3,4]. The previous generation of that generator has been extensively studied. This article and research provides the first catalogue of treatment dose recommendations for CAP generated by the current generation CHCP XL1000 2-in-1 combination electrosurgical generator and conversion unit. The effectiveness of this generator to reduce viability in a variety of solid tumor types is of interest as it is subject to a phase 1 FDA Investigational Device Exemption Approval clinical trial in Israel and in the United States. The trial investigated the safety and efficacy of CHCP on numerous cancer types during cytoreductive surgery. The cell viability results in this study provided a guideline for the dose used in the clinical trial for corresponding cancers such as cholangiocarcinoma, renal adenocarcinoma, lung, colon, and ovarian carcinomas.

Cell Viability

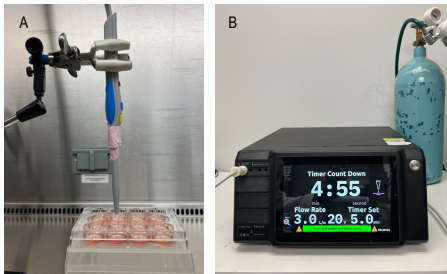


Figure 1: A) Canady Helios Cold Plasma (CHCP) 2-in-1 combination electrosurgical setup during treatment B) Canady Helios Cold Plasma Scalpel (CHCPS) setup for treatment of cell lines

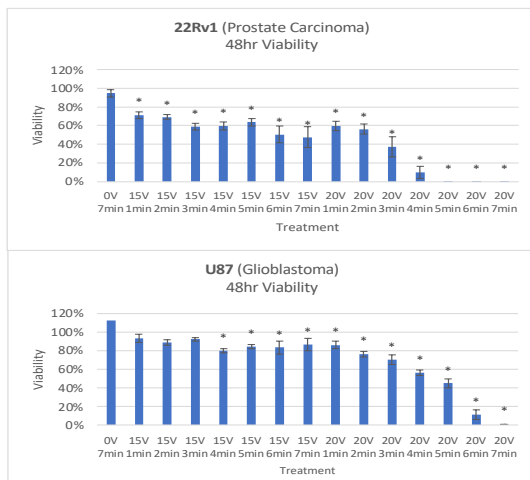


Figure 2: Cell viability reduction of A) 22Rv1 and B) U87 after CHCP treatment for 1–7 min at 15V and 20V compared to untreated controls. * p<0.05

Table 1: Recommended CHCP power settings and treatment duration for different cancer types required to achieve an 80-99% reduction in cell viability. The flow rate for all treatments was 3 L/min of helium.

Tissue	Cell Line	Power Settings (V)	Treatment duration (min)	Viability (%)
Breast	MDA-MB-231	20	3	9
Breast	Sk-Br-3	20	4	1
Breast	MCF-7	20	7	1
Liver	KKU-055	20	5	2
Colon	HCT-116	15	2	8
Stomach	AGS	20	4	8
Stomach	SNU-1	20	5	7
Brain	U-87	20	7	1
Liver	Hep G2	20	7	8
Lung	A549	20	7	8
Skin	SK-MEL-28	20	6	1
Skin	A-375	20	4	2
Ovary	SK-OV-3	20	7	18
Pancreas	BxPC-3	20	4	1
Prostate	22Rv1	20	5	1
Kidney	769-P	20	3	1
Thyroid	8505c	20	5	9
Esophagus	OE33	20	4	3
Esophagus	OE21	20	4	3
Rectum	SW837	20	7	6

To understand CHCP dosimetry, 20 solid tumor cell lines were treated with CHCP at 0, 15 and 20 V for 1 - 7 minutes (Figure 1, Table 1). This treatment duration was chosen to model device use in a clinical setting. MTT assays were used to measure cell viability 48 hours after treatment. The viability of all cell lines were reduced in a dose-dependent manner with each cancer type requiring a slightly different power and time setting. A selection of cell line MTT assay results are shown in Figure 2. Cell lines like the prostate carcinoma 22Rv1 and glioblastoma U87 were completely eradicated by 20V CHCP 20V for 5 and 7 minutes, respectively. In each cell line 80-99% viability reduction was achieved compared to non-treated cells (Table 1). Treatment doses followed a similar pattern where the lower power of 15V was less effective in reducing viability than 20V (Figure 2). Similarly, longer treatment times of 5-7 minutes were more effective than shorter treatment times.

Conclusion

Our data demonstrates that CHCP is an effective treatment for a wide variety of tumors. Insights from these viability studies are critical to understand the CHCP recommended dosage *in vivo*. This ensures that the appropriate CAP dose for treating a specific cancer type is used during surgery. There is tremendous potential for the application of CHCP as a targeted therapy for different cancers as the technology translates to the clinical field.

References

- Semmler, M.L., et al., *Molecular Mechanisms of the Efficacy of Cold Atmospheric Pressure Plasma (CAP) in Cancer Treatment*. *Cancers (Basel)*, 2020, 12(2).
- Bernhardt, T., et al., *Plasma Medicine: Applications of Cold Atmospheric Pressure Plasma in Dermatology*. *Oxid Med Cell Longev*, 2019, 2019: p. 3873928.
- Ly, L., et al., *Canady cold plasma conversion system treatment: An effective inhibitor of cell viability in breast cancer molecular subtypes*. *Clinical Plasma Medicine*, 2020.
- Rowe, W., et al., *The Canady Helios Cold Plasma Scalpel Significantly Decreases Viability in Malignant Solid Tumor Cells in a Dose-Dependent Manner*. *Plasma*, 2018, 1(1): p. 177-188.