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Effect of Ionizing Radiation on the Physical Biology of Head and Neck Squamous Cell Carcinoma Cells

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Abstract

Head and neck squamous cell carcinoma (HNSCC) is the sixth leading cause of cancer worldwide. Although there are numerous treatment options for HNSCC, such as surgery, cytotoxic chemotherapy, molecularly targeted systemic therapeutics, and radiotherapy, overall survival has not significantly improved in the last 50 years. This suggests a need for a better understanding of how these cancer cells respond to current treatments in order to improve treatment paradigms. Ionizing radiation (IR) promotes cancer cell death through the creation of cytotoxic DNA lesions, including single strand breaks, base damage, crosslinks, and double strand breaks (DSBs). As unrepaired DSBs are the most cytotoxic DNA lesion, defining the downstream cellular responses to DSBs are critical for understanding the mechanisms of tumor cell responses to IR. The effects of experimental IR on HNSCC cells beyond DNA damage in vitro are ill-defined. Here we combined label-free, quantitative phase and fluorescent microscopy to define the effects of IR on the dry mass and volume of the HNSCC cell line, UM-SCC-22A. We quantified nuclear and cytoplasmic subcellular density alterations resulting from 8 Gy X-ray IR and correlated these signatures with DNA and γ -H2AX expression patterns. This study utilizes a synergistic imaging approach to study both biophysical and biochemical alterations in cells following radiation damage and will aid in future understanding of cellular responses to radiation therapy.

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Keywords—Quantitative phase microscopy, Radiation damage, Physical biology, Head and neck squamous cell carcinoma.

ABBREVIATIONS

HNSCC	Head and neck squamous cell carcinoma
IR	Ionizing radiation
DSB	Double strand breaks
BSA	Bovine serum albumin
PBS	Phosphate buffered saline
NA	Numerical aperture
DIC	Differential interference contrast
HTDIC	Hilbert-transform differential interference contrast
NIQPM	Non-interferometric quantitative phase microscopy
FWHM	Full-width at half maximum

INTRODUCTION

Head and neck cancers are typically squamous cell carcinomas that present in the larynx, pharynx, salivary glands, nasal cavity, paranasal sinuses, or oral cavity. Worldwide, head and neck squamous cell carcinomas (HNSCCs) are responsible for 250,000 annual deaths and have a mortality rate of approximately 50%.¹⁰ Current treatments for HNSCC consist of chemotherapy, surgery, molecular targeted therapy, radiation therapy, or a combination thereof. While the epidemiology and pathogenesis of HNSCC has been well defined in recent years; only minimal improve-

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About this Article

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