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Silicon Nanotweezers with a microfluidic cavity for the real time characterization of DNA damage under therapeutic radiation beams

Grégoire Perret, *Student Member, IEEE,* Po-Tsun Chiang, Thomas Lacornerie, Momoko Kumemura, Nicolas Lafitte, Herve Guillou, Laurent Jalabert, Eric Lartigau, Teruo Fujii, Fabrizio Cleri, Hiroyuki Fujita *Member, IEEE*, and Dominique Collard, *Member*

***Abstract*—We report the biomechanical characterization of λ-DNA bundle exposed to a therapeutic radiation beam by silicon Nanotweezers. The micromechanical device endures the harsh environment of radiation beams, and still retains molecular-level detection accuracy. The real-time DNA bundle degradation is observed in terms of biomechanical stiffness and viscosity reduction, both in air and in solution. These results pave the way for both fundamental and clinical studies of DNA degradation mechanisms under ionizing radiation for improved tumor treatment.**

I. Introduction

Tumor cell killing by γ-ray beams in cancer radiotherapy is currently based on a rather empirical understanding of the basic mechanisms and effectiveness of DNA damage by radiation [1]. On the other hand, the mechanical behavior of DNA, e.g., sequence–sensitivity, elastic vs. plastic response, is well understood [2]. However, manipulations are usually performed by AFM or optical tweezers, instruments that can hardly be placed and operate under radiation beams.

II. Methods

The Silicon Nano Tweezers (SNT) is a MEMS device for direct manipulation of biomolecules [3], an excellent candidate for in-beam operation thanks to its tiny size. The SNT (Fig.1(a)) comprise two parallel arms ending with sharp tips, designed to trap molecules by dielectrophoresis [4]. The mechanical characteristic of the trapped molecules (stiffness, viscosity) are measured in real time. The SNT could be inserted inside a microfluidic cavity (Fig. 1(b)) in order to allow indirect DNA damage due to radicals produced by H_2O irradiation.

The experiments are performed with a Cyberknife, a LINAC accelerator mounted on a robot arm. (Fig.1(a)).

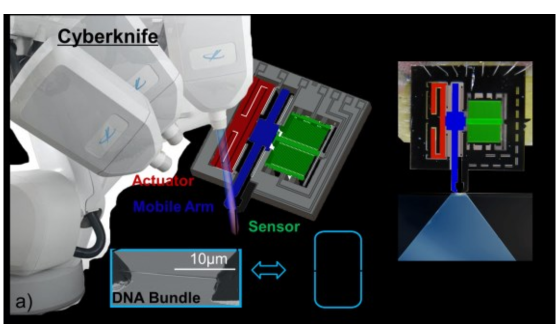

Fig 1. SNT under Cyberknife in microfluidic cavity

III. Results

To study the capability of SNT to perform biomechanical sensing of the DNA degradation under X-ray, two steps are reported here. A first one consisted in checking the noise level generated by the 6 MeV radiation on the bare SNT; the second we tested the capability to perform the irradiation assay with the DNA bundle immersed in a microfluidic cavity, and the ability to detect its alteration. In all experiments, we used bundles of λ-DNA of 48.5 kbp, for a contour length of 16µm; a typical bundle contains about 5000 identical ds-DNA strands. Notably, the gap of the SNT is in the range of 10 µm, therefore the DNA molecules are held and straightened between the SNT tips for a meaningful fraction of their contour length.

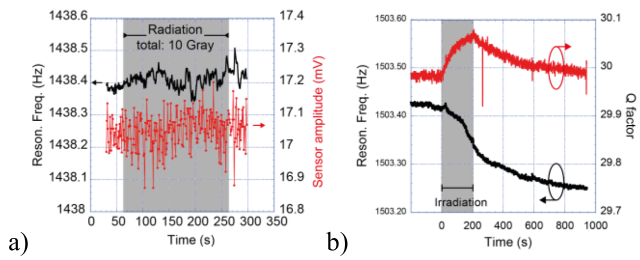

Fig 2. a) Noise level b) DNA bundle degradation under irradiation

IV. Conclusions

Silicon Nanotweezers operation under therapeutic irradiation and direct detection of DNA damage under γ-ray beam was first demonstrated. **Coupled with microfluidics**, this new capability permits to study the mechanics of DNA damage under ionizing beams for optimized tumor treatment.

References

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