SILICON NANO TWEEZERS FOR REAL TIME BIOMECHANICAL ASSAY ON DNA DAMAGE BY THERAPEUTIC RADIATION BEAMS

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ABSTRACT

We report the biomechanical characterization of a λ-DNA bundle exposed to a therapeutic radiation beam by Silicon Nanotweezers. The device endures the harsh environment of radiation beams and still retains molecular-level accuracy. This result paves the way for both fundamental and clinical studies of DNA degradation mechanisms under ionizing radiation for improved tumor treatment.

KEYWORDS
Silicon Nano tweezers, Radiation therapy, Molecular manipulation, DNA characterization

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.

EXPERIMENT

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) comprise two parallel arms ending with sharp tips, designed to trap molecules by dielectrophoresis. The mobile arm is displaced by an electrostatic actuator. The motion is acquired by a position sensor, thus the mechanical characteristic of the trapped molecules (stiffness, viscosity) are measured in real time.

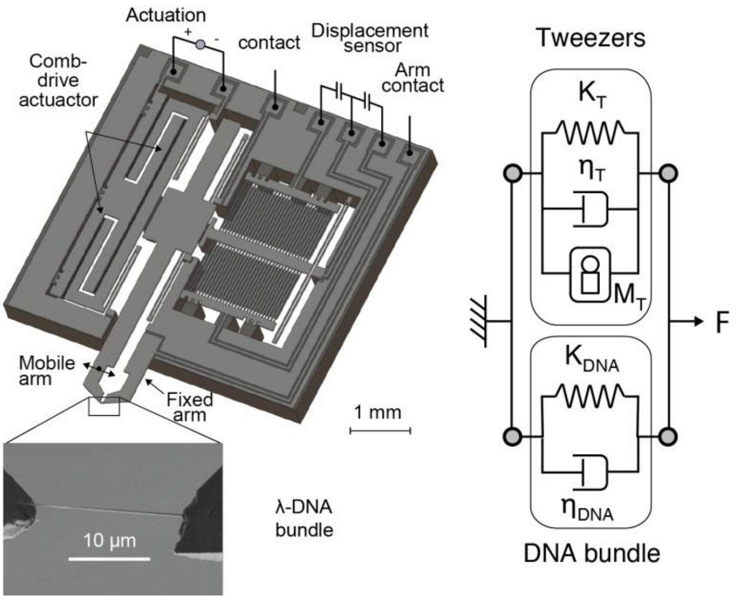

Figure 1: Silicon Nanotweezers, close-up view on a trap DNA bundle. Equivalent damped Oscillator model.

The experiments are performed with a Cyberknife, a LINAC accelerator mounted on a robot arm, at the Department of Radiation Therapy of Centre Oscar Lambret (fig. 2). The SNT is placed under the Cyberknife head, (fig.2a). The collimated beam, delivering an intense 6 MeV photon flux, completely encompasses the SNT holding the DNA bundle. The electronics is put 1.5 m away from the beam.

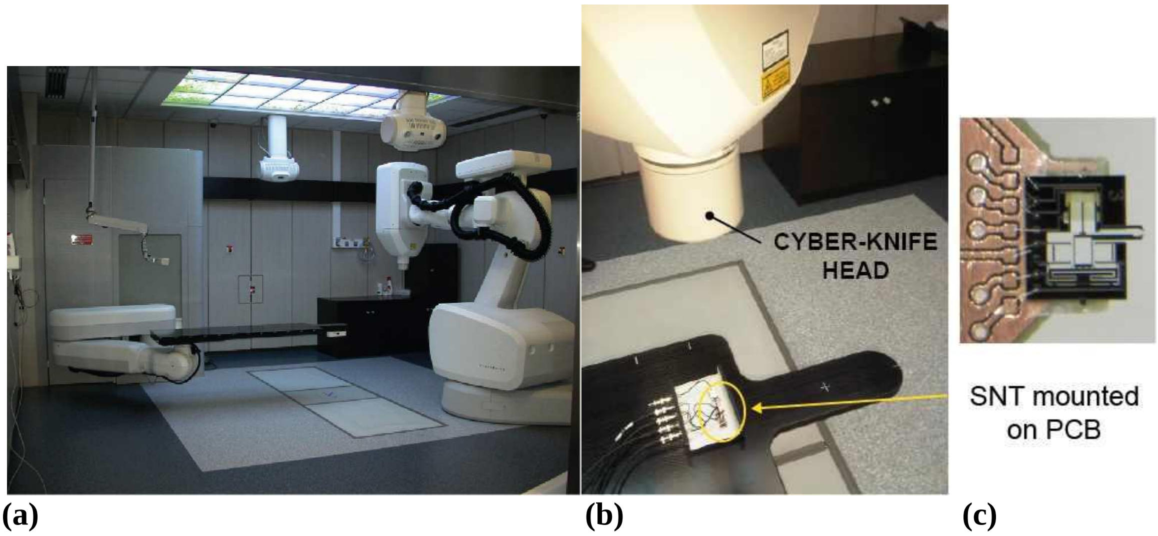

Figure 2: (a) CyberKnife machine in Centre Oscar Lambret, Lille, France used for the experiments. (b) Experimental set-up. The SNT is under the radiation beam generated by the CyberKnife head. (c) Picture of the SNT showing the grounded connection to the lock-in amplifier (not shown).

The frequency responses of the SNT, before, during and after the irradiation are plotted in Fig. 3(a). The curves perfectly superposed, revealing whole of the SNT, its silicon material, and the electronic connections, are perfectly resistant to the radiation dose. The second test reveals the stability of the SNT resonance. Once the SNT is locked to its own resonant frequency, the LINAC radiation beam is turned on for 200 s (total dose 10 Gy). The resonant frequency (F_R) and associated peak values are recorded and plotted in Fig. 3(b). The noise levels are not significantly modified under irradiation, thus molecular-level accuracy is kept for mechanical measurement (threshold: 10 ds-DNA).

The first measurement of dried DNA-bundle damage under Cyber-Knife irradiation was carried out. A thin DNA bundle was trapped [4] and placed under the photon beam, and irradiated. The SNT F_R and Q factors are recorded in real time. The F_R decrease (reduced stiffness) and Q increase (reduced viscosity) show the damages of the DNA (insert of Fig.4). The evolution of the DNA stiffness, calculated from the oscillator model(fig.1b) shows a first order kinetics of the DNA degradation.

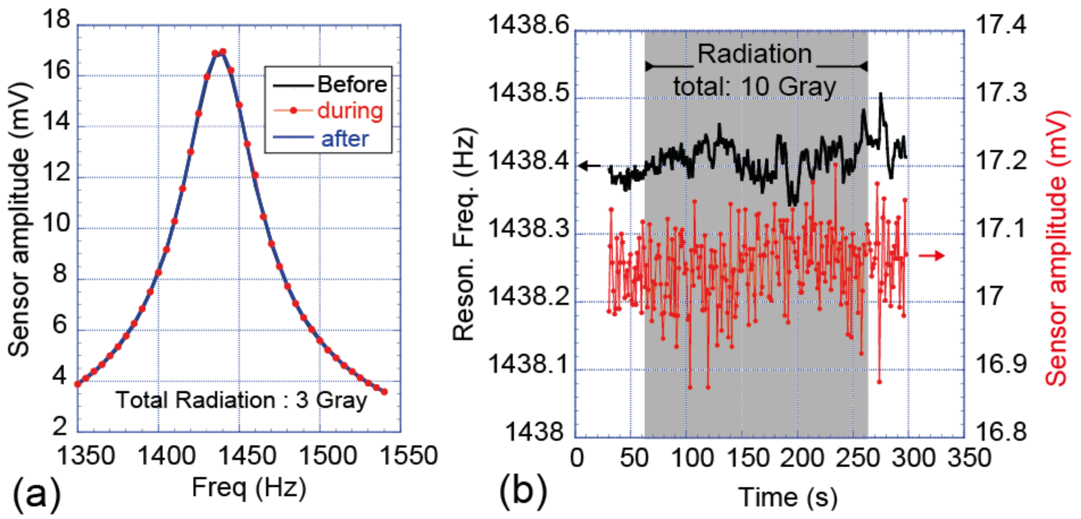

Figure 3: (a) Frequencies response of bare SNT. (b) Locked resonance frequencies and associated peak values during the irradiation

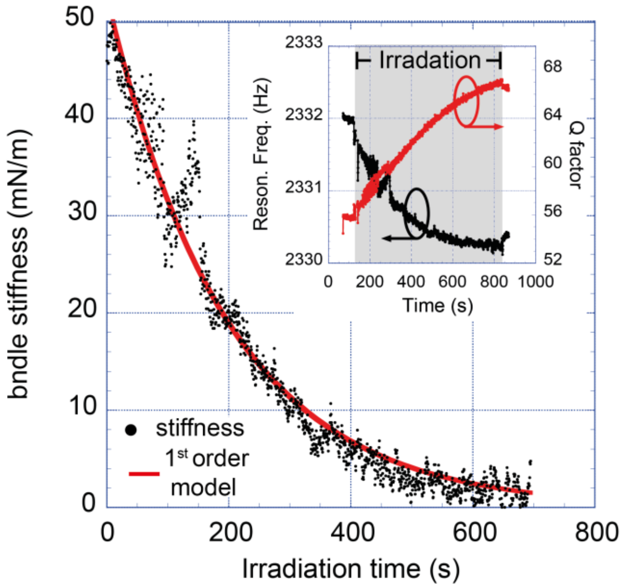

Figure 4: Mechanical characterization of the bundle damage in air during irradiation (total 100Gy with 4 ms pulses at 300 Hz, dose-rate of 8 Gy/min). Decrease of the bundle stiffness K_{DNA} with time and kinetics extraction. Insert: Measured SNT Response resonance frequencies and Q factor.

RESULTS

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.

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