# REAL TIME MECHANICAL CHARACTERIZATION OF DNA IN LIQUID DURING A RADIOTHERAPY TREATMENT AND ITS THEORETICAL ANALYSIS

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## ABSTRACT

**We report the first real-time biomechanical measurement of DNA bundle degradation in stable condition when exposed to a therapeutic radiation beam and a theoretical model to describe DNA damages. The Silicon Nano Tweezers and their new microfluidic system endure the harsh environment of radiation beams and still retain molecular-level accuracy. This result paves the way for both fundamental and clinical studies of DNA degradation under radiation for improved tumor treatment.**

## INTRODUCTION

Tumor cell killing by gamma-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.

## METHODS

The Silicon Nano Tweezers (SNT) is a MEMS device for direct manipulation of biomolecules, an excellent candidate for in-beam operation thanks to its tiny size. The SNT (Fig.1) comprise two parallel arms ending with sharp tips, to trap molecules by dielectrophoresis.

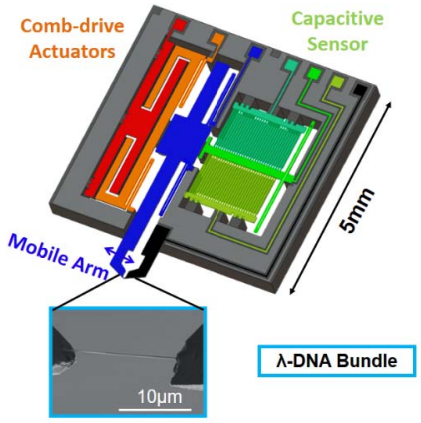


*Figure 1: Silicon Nanotweezers, close-up view on a trap DNA bundle.*

The mobile arm is displaced by an electrostatic actuator. The motion is acquired by a position sensor, thus the mechanical characteristic (Fig.2) of the molecules (stiffness, viscosity) are measured in real time.

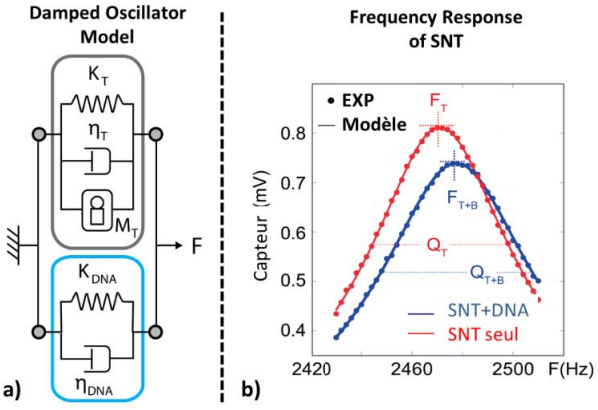


*Figure 2: a) Equivalent damped Oscillator model b) Frequency response of SNT with and without DNA bundle inside fluidic cavity.*

**SNT's tips are placed inside a microfluidic cavity; and different medium could be used.** The stability of the system depend on the size of the microfluidic aperture. At this dimension, **the insertion should be controlled** by a micro-robot (Fig.3).

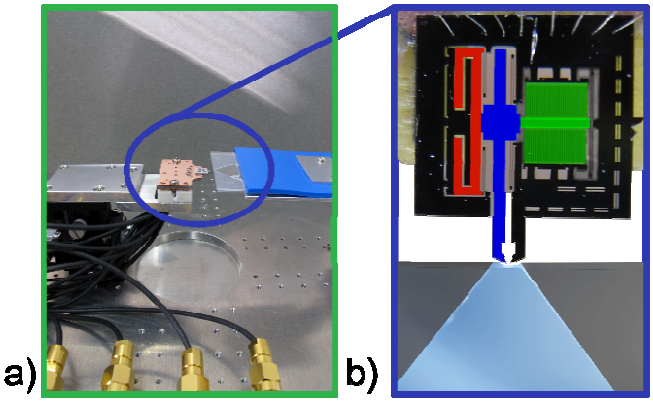


*Figure 3: a),b) Zoom on the SNT + fluidic cavity controlled by a micro-robot. The system is under the radiation beam generated by the CyberKnife head.*

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.4). **The SNT inside a microfluidic cavity** is placed under the Cyberknife. The collimated beam, delivering an intense 6 MeV photon flux, completely encompasses the SNT holding the DNA bundle in the microfluidic cavity.

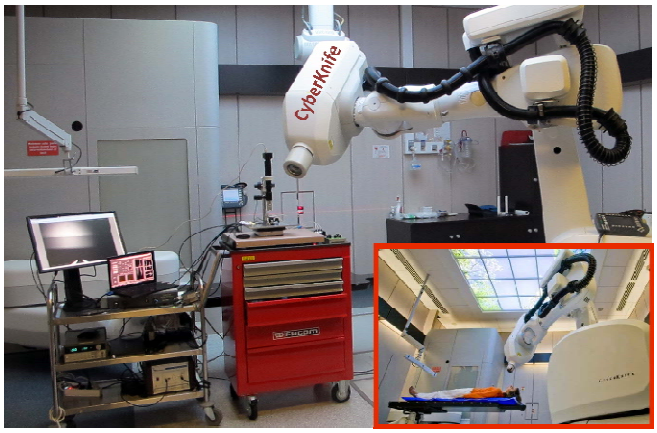


*Figure 4: Overview of the experimental set-up with the CyberKnife machine in Centre Oscar Lambret, Lille, France used for the experiments.*

## RESULTS AND DISCUSSIONS

For all experiments, the SNT **is inserted inside a microfluidic cavity** before the irradiation then LINAC radiation beam is turned on (30Gy). Both, the resonant frequencies and the amplitude of the SNT are plotted in Fig.5. First, SNT without DNA was irradiated to get a reference and shown that SNT are perfectly resistant to the radiation dose. Then DNA bundle was trapped [3], and **the system SNT+DNA endured for the first time fractionated irradiations**. To analyze data and to be able to compare different experiments with different DNA bundles, the stiffness is calculated from the oscillator model (Fig.2) and plotted with the equivalent number of DNA molecules which composed the bundle (Fig.5).

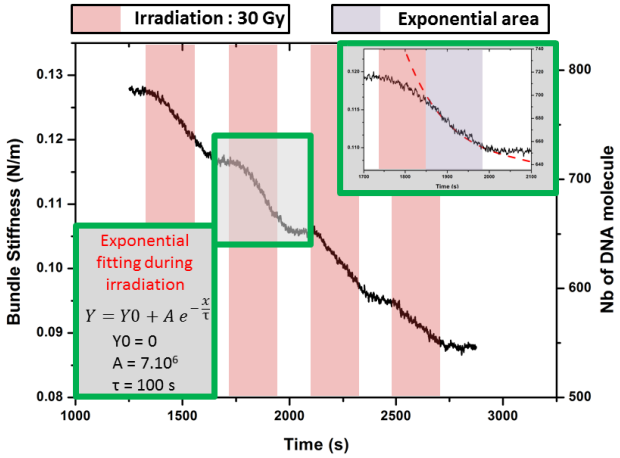


*Figure 3: 4x30Gy irradiation (4 ms pulses at 300 Hz) on same DNA bundle. Zoom on 2nd irradiation and exponential fitting.*

This experiment on a unique DNA bundle shows a short term repeatability and provides a kinetic of DNA degradation.

Our **novel theoretical approach** to describe the effective Young's modulus degradation in a fiber bundle subjected to an external damaging action confirm that the homogenized bundle stiffness exhibits an exponential degradation Fig.6, which is controlled by the fracture density and by the fibers interaction.

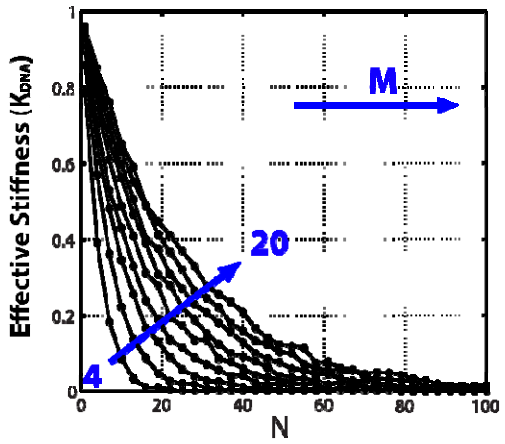


*Figure 6: Simulation of a bundle of M fibers viscously link. Effective stiffness (real part of the Young modulus) vs number of break (N). It confirms the exponential dependency find during the experiment.*

## CONCLUSION

Measurement of DNA damage under gamma-ray beam was first demonstrated. The repeatability and the theoretical analysis permit to study the mechanics of DNA damage under irradiation for optimized tumor treatment. Modeling of the DNA degradation allow to quantify the protocol for clinical research objective.

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*Figure 10: International multidisciplinary team with MEMS specialist Engineer, Physicists, Biologist and Medical Doctor, during DNA Irradiation experiment with the CyberKnife machine in Centre Oscar Lambret, Lille, France.*

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