

How Compact Spectrometers are being used in Cancer Research: Approaches to a Multifaceted Problem

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Every week, it seems like another friend or family member is diagnosed with cancer. The [American Cancer Society predicts](#) that 1,688,780 people will be diagnosed with cancer and 600,920 people will die from cancer in the US in 2017. This problem isn't limited to the US, either. The [World Cancer Research Fund International estimates](#) that there were 14.1 million cancer cases worldwide in 2012. Aside from the obvious humanitarian aspect of this problem, it's also a huge economic burden. The [American Cancer Society estimates](#) that cancer related health care costs were \$87.8 billion in 2014.

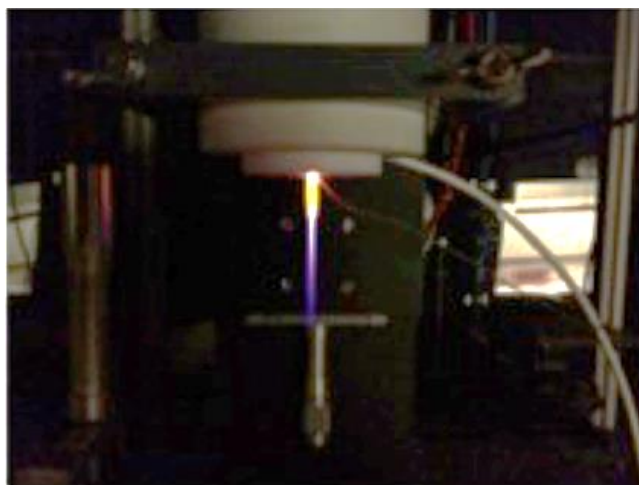
Clearly this is a worldwide problem. Why is a solution so difficult? The word "cancer" actually includes many diseases, each with their own set of characteristics and treatment. They have a common mechanism, though: somehow, normal cells start behaving erratically and grow out of control, preventing other cells from performing their function. This presents two main problems: One, cancer cells end up being very similar to normal cells as far as treatments go. This means finding treatments that are specific to cancer cells is difficult. Two, the cause of cells turning cancerous is complex and difficult to pinpoint for prevention or targeted treatment.

Still, cancer researchers persist. Here is a collection of studies by StellarNet's customers.

Treatments Using Low Temperature Plasma Devices

The Keidar group at George Washington University, as well as the Yang group at the Chinese Academy of Sciences, have both been working with plasma devices for treating cancer. The specific devices are low temperature, meaning they can be used in biological systems, and operate at atmospheric pressure, meaning expensive vacuum equipment is not necessary.

The Yang group uses a nozzle to force the plasma discharge into a needle that allows for spacial precision in the plasma application [1,2]. In one study, you can see a clear boundary between human lung cancer A549 cells that are still viable and dead cells that were directly under the plasma needle [1]. With optimum plasma conditions, the lung cancer cells had a 6% survival rate. The plasma needle also gave good results with BEL-7402 liver cancer cells [2]. In both studies, the authors used an [BLACK-Comet](#) spectrometer to collect the UV-vis spectrum of the plasma discharge itself and the amount of discharge emission that



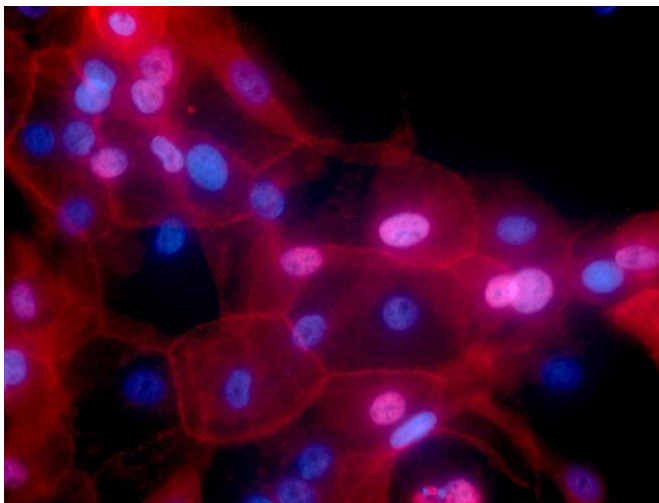
A plasma needle device. Adapted from Figure 1 in Ref. [8].

reached the cells in the medium [1,2].

The discharge, formed with Ar and O gases, showed peaks for NO, OH, N₂, N, Ar, and O. However, the NO and N₂ peaks disappear inside the media. This suggests that the nitrogen radicals produced by the discharge are absorbed by the media and that the oxygen radicals are the ones that diffuse to the cells and cause ablation.

The Keidar group has experimented with two types of plasma devices. The first is actually a combination of plasma with a static magnetic field [3]. The authors used a StellarNet spectrometer and probe to measure the emission spectrum of the plasma with and without the static magnetic field; the spectra were identical, proving that the field did not alter the plasma. They then treated breast cancer MDA-MB-231 cells with four treatments:

1. direct plasma treatment (cells were present when the plasma was applied) only
2. direct plasma treatment + static magnetic field
3. indirect plasma treatment (plasma was applied to the media and then cells added) only
4. indirect plasma treatment + static magnetic field



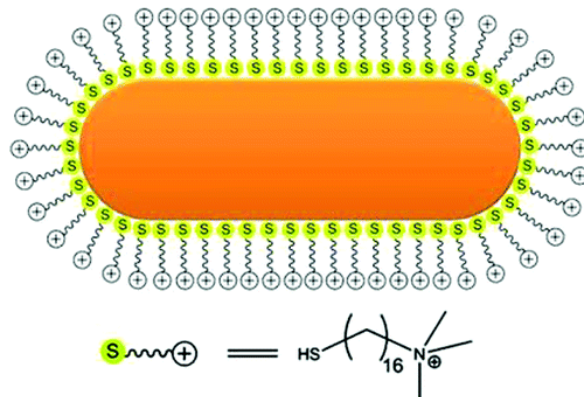
Breast cancer cells. Figure by Ewa Krawczyk,
<https://visualsonline.cancer.gov/details.cfm?imageid=10623>.

Treatment 2 performed the best; it was 8.5 times more likely to kill cancer cells than normal cells! The second device was an atmospheric pressure microdischarge plasma device [4]. It created self organized patterns on the interface between the plasma and the medium. At low current and voltage (Type I), the plasma created only one filament at the interface (similar to the needle), but high current and voltage (Type IV) produced many filaments. They again used StellarNet products to collect the emission spectra, which were similar. Both types were able to decrease the survival rate of breast cancer MDA-MB-231 cells and glioblastoma U87 cells, but had more of an effect on the glioblastoma cells. The high current stage actually cause the reactive oxygen species to decrease over time, which

is the opposite behavior observed for most other plasma devices.

Gold Nanoparticles for Photothermal Ablation

Another popular idea for treatment is photothermal ablation by using nanoparticles. Rossi *et. al.* used a software package called COMSOL to model the heat generated by gold nanorods as they were irradiated at 810 nm [5]. The model required the absorption cross section of the nanoparticles, which the authors measured with a [BLUE-Wave](#) spectrometer. One model was nanoscale to examine the local



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temperature environment around the nanorods when placed in a biopolymeric shell. The optimal laser conditions to achieve hyperthermia without degrading the sample were 0.5 mW/cm₂ for 2s. They also created a microscale model where the nanorod and shell were placed in a tumor. This revealed that the heat effects were highly local, so multiple clusters of nanorods would be needed to affect a tumor.

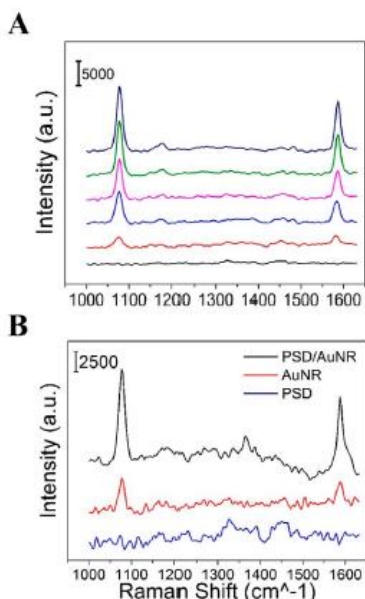


Figure 5. (A) SERS spectra of 4-MBA in PSD/AuNR water solutions at various concentrations (from top to bottom: 10⁻³, 10⁻⁴, 10⁻⁵, 10⁻⁶, 10⁻⁷, and 10⁻⁸ M). (B) SERS spectra of 10⁻⁴ M 4-MBA on PSD/AuNR, AuNR, and PSD in aqueous solutions.

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Skin Lesion Classification

Before cancer can be treated, it needs to be diagnosed.

Melanoma is one type of cancer that is tricky to diagnose. Currently, dermatologists have to rely on their own visual inspection to determine if skin lesions should be biopsied. Technology can help streamline this process and possibly help avoid biopsies altogether. Safi *et al.* used reflectance spectroscopy

along with machine learning to come up with a model for predicting if a lesion is harmful or not [7]. They used a [BLACK-Comer-SR](#) spectrometer with a 12W tungsten lamp and reflectance



One thing that Rossi *et al.* neglected was ligands, which has been one of the roadblocks for nanoparticle based treatments. Nanoparticles need ligands to stabilize in solution and these ligands are often toxic. Zhu *et al.* solved this by creating gold nanorods inside of porous silica nanodisks (abbreviated as PSD/AuNR) [6]. With the silica acting as a support framework, ligands weren't needed for stabilization. This new particle is a biological jackknife; the nanoparticles can be used for photothermal ablation, the particle can be used for drug delivery, and the distribution of the nanoparticles makes it a great SERS substrate! The authors used a StellarNet Raman system at 785nm to take the SERS spectra. Some example spectra are reprinted to the left. The particle was also effective at killing human pancreatic carcinoma cells PANG1 and MIA PaCa-2 when used for photothermal ablation and chemotherapy drug delivery simultaneously.



probe to measure the reflectance spectra of lesions. A principal components analysis (PCA) was used to decrease the dimensionality of the dataset and then it was input into a support vector machine (SVM) algorithm. This algorithm is good for finding decision boundaries between classes when said boundaries are likely to be nonlinear. This is achieved by transforming the nonlinear data with a kernel to a new vector space where the boundary *is* linear. Then the calculated boundary is transformed back to the original space. The authors used cross validation to determine that using radial basis functions as the kernel and using the top 4 or 5 principle components gave the best accuracy; both combinations were able to classify the lesions with 94.9% accuracy.

Cancer is an extremely complex problem, but researchers are extremely dedicated. With a world full of scientists looking for a solution, it's only a matter of time before a complete solution is found.

References

1. Huang J, Chen W, Li H, Wang X-Q, Lv G-H, Khohsa ML, et al. Deactivation of A549 cancer cells in vitro by a dielectric barrier discharge plasma needle. *J Appl Phys.* 2011;109: 053305.
2. Zhang X, Li M, Zhou R, Feng K, Yang S. Ablation of liver cancer cells in vitro by a plasma needle. *Appl Phys Lett.* 2008;93: 021502.
3. Cheng X, Rajjoub K, Shashurin A, Yan D, Sherman JH, Bian K, et al. Enhancing cold atmospheric plasma treatment of cancer cells by static magnetic field. *Bioelectromagnetics.* 2017;38: 53–62.
4. Chen Z, Zhang S, Levchenko I, Beilis II, Keidar M. In vitro Demonstration of Cancer Inhibiting Properties from Stratified Self-Organized Micro-Discharge Plasma-Liquid Interface [Internet]. *arXiv.* 2017. Available: <https://arxiv.org/abs/1701.01655>
5. Rossi F, Ratto F, Pini R. Laser Activated Gold Nanorods for the Photothermal Treatment of Cancer. *COMSOL*; Available: <https://www.comsol.com/paper/laser-activated-gold-nanorods-for-the-photothermal-treatment-of-cancer-13260>
6. Zhu G, Liu J-T, Wang Y, Zhang D, Guo Y, Tasciotti E, et al. In Situ Reductive Synthesis of Structural Supported Gold Nanorods in Porous Silicon Particles for Multifunctional Nanovectors. *ACS Appl Mater Interfaces.* 2016;8: 11881–11891.
7. Safi A, Castaneda V, Lasser T, Navab N. Skin Lesions Classification with Optical Spectroscopy. In: Liao H, Edwards PJ “eddie,” Pan X, Fan Y, Yang G-Z, editors. *Medical Imaging and Augmented Reality.* Berlin, Heidelberg: Springer Berlin Heidelberg; 2010. pp. 411–418.
8. Virard F, Cousty S, Cambus J-P, Valentin A, Kémoun P, Clément F. Cold Atmospheric Plasma Induces a Predominantly Necrotic Cell Death via the Microenvironment. *PLoS One.* 2015;10: e0133120.
9. Bao Y, Vigderman L, Zubarev ER, Jiang C. Robust multilayer thin films containing cationic thiol-functionalized gold nanorods for tunable plasmonic properties. *Langmuir.* 2012;28: 923–930.