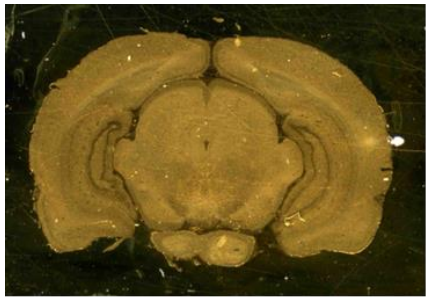
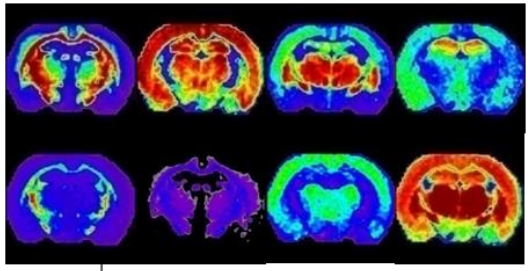
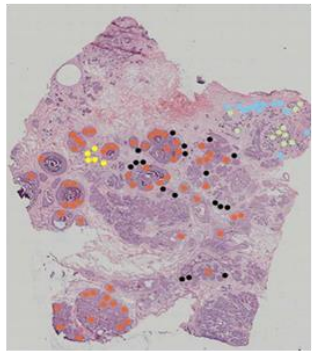
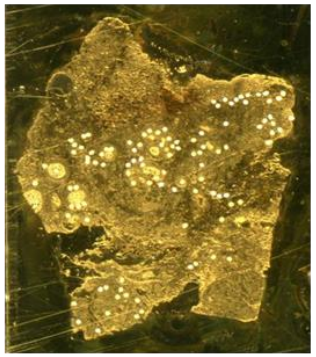
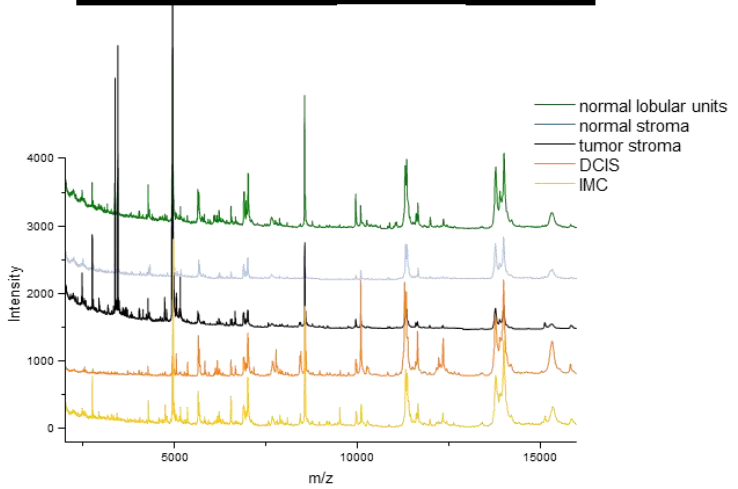
Biofluid and Cytology Profiling

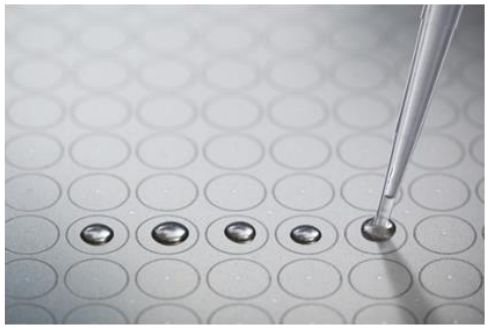


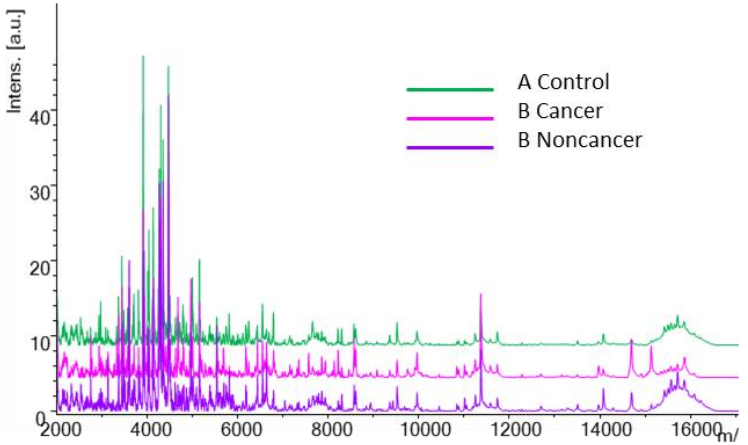








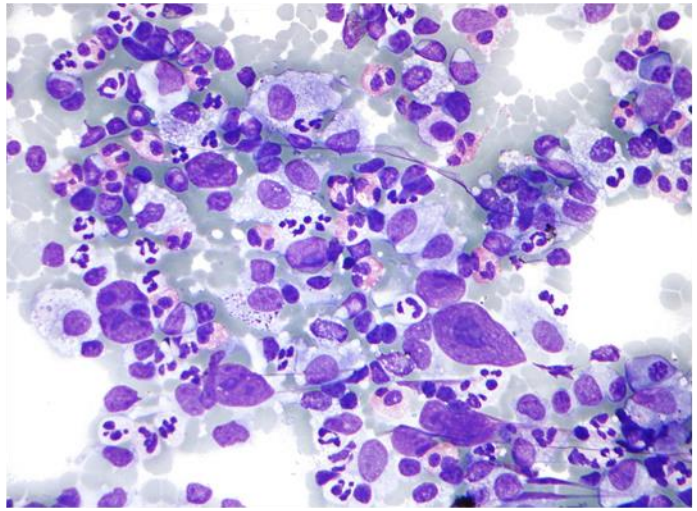


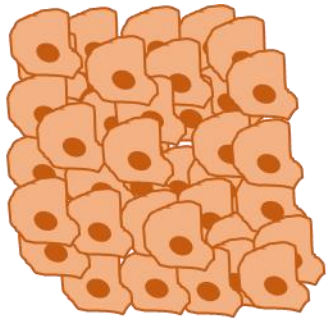


Biofluid/Cytology Profiling - Overview

In addition to traditional tissue analysis, mass spectrometry profiling can also be applied to biofluid and cytology specimens. In the case of biofluids, the fluid analyzed should be directly related to the disease being study. This may include examples like urine profiling for bladder cancer or cerebrospinal fluid profiling for neurological cancers or disorders. Serum/plasma profiling has shown limited utility due to the high dynamic range of biomolecules and relatively low abundance of markers of interest.

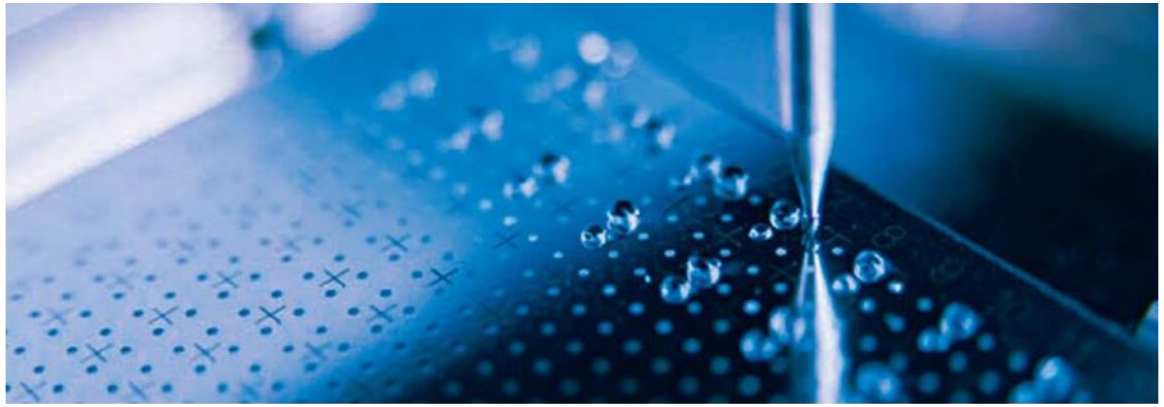
MS profiling can also be applied to cytology specimens such as fine needle aspirates, scrapes/smears, liquid biopsies, and cell cultures. These samples may be lysed and analyzed in a similar manner to biofluids or deposited on slides to be analyzed using tissue-like methodologies.

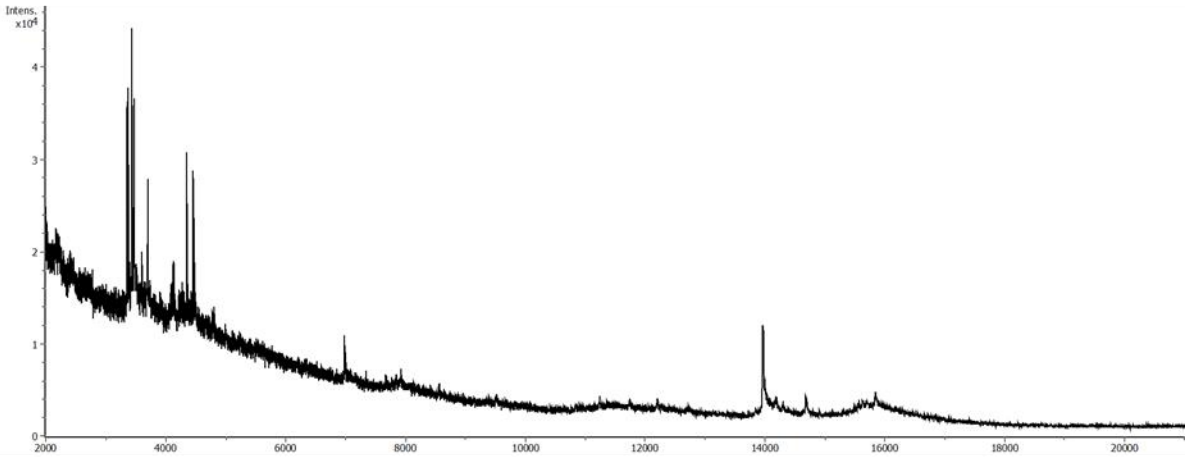




Biofluid Profiling – “Dilute-n-Shoot”

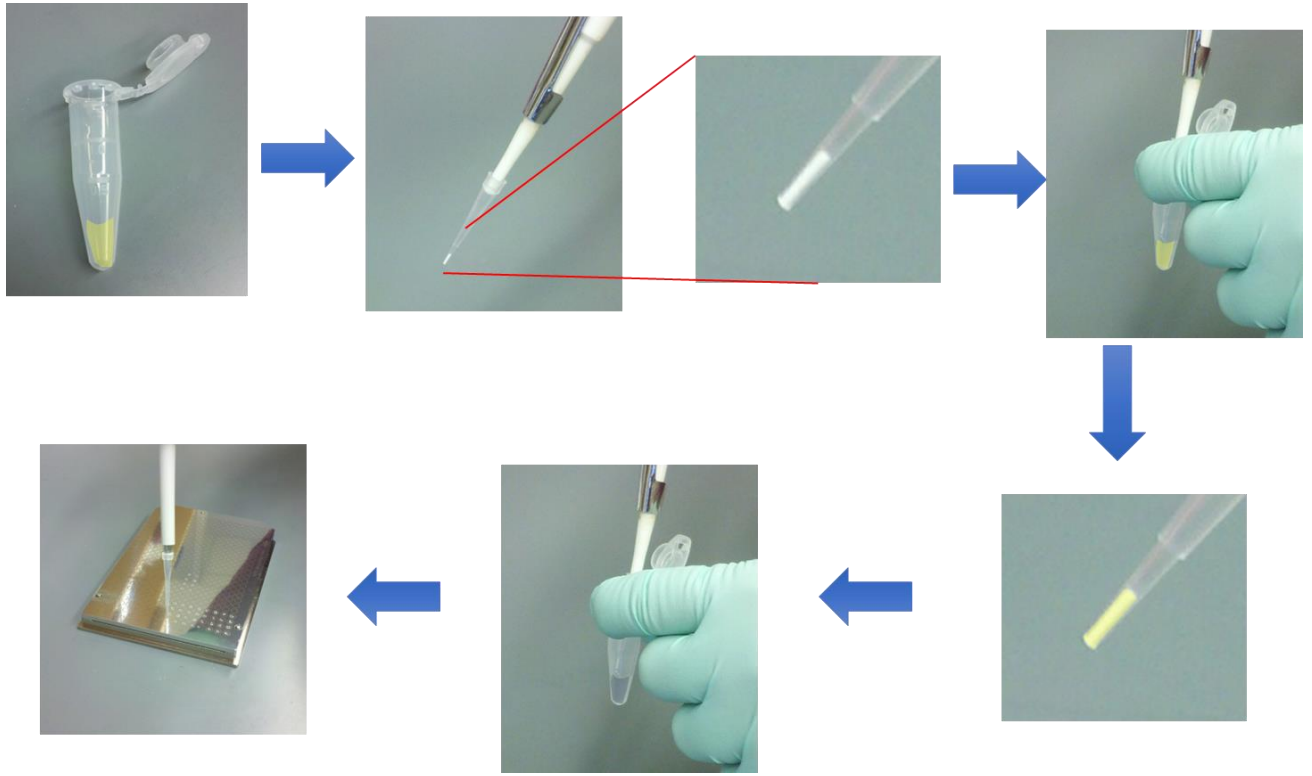
The simplest type of biofluid analysis is what is commonly referred to as “dilute-n-shoot”. As the name implies, the sample is simply subjected to a dilution with solvent before being spotted to a target and analyzed. The dilution of the sample helps to achieve an appropriate biomolecule concentration range for detection in the mass spectrometer as well as decreasing the salt concentration in the sample, which can suppress the signal from analytes of interest. The “dilute-n-shoot” method has shown limited utility due to the reduced number of detected peaks as compared to more sophisticated sample preparation approaches. The spectra tend to be somewhat noisy with a high observed baseline.





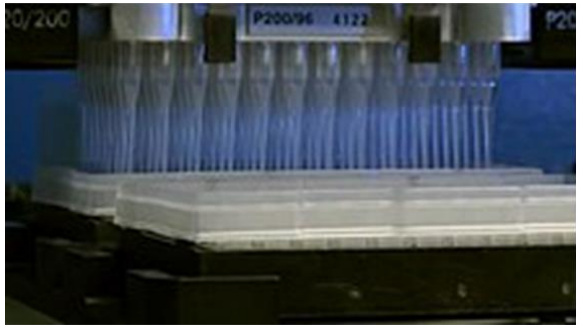
Biofluid Profiling – 1D Cleanup

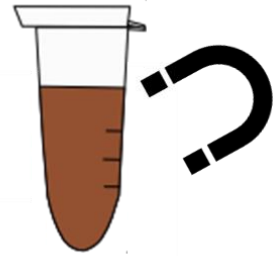
The most common approach for biofluid profiling is to perform a 1-dimensional cleanup of the samples or desalting. This cleanup is typically carried out using pipet tips packed with a stationary phase or through the use of functionalized magnetic beads. The sample is passed over the stationary phase where the molecules of interest are non-covalently bound. The stationary phase is washed to remove non-bound molecules such as salts. A different solvent is then passed over the stationary phase to elute the bound analytes which are subsequently spotted to a target for mass spectral analysis. In addition to removing salts from the samples, 1D cleanup also serves to normalize the total amount of analyte being detected from each sample through saturation of the stationary phase.



Biofluid Profiling – 2D Fractionation

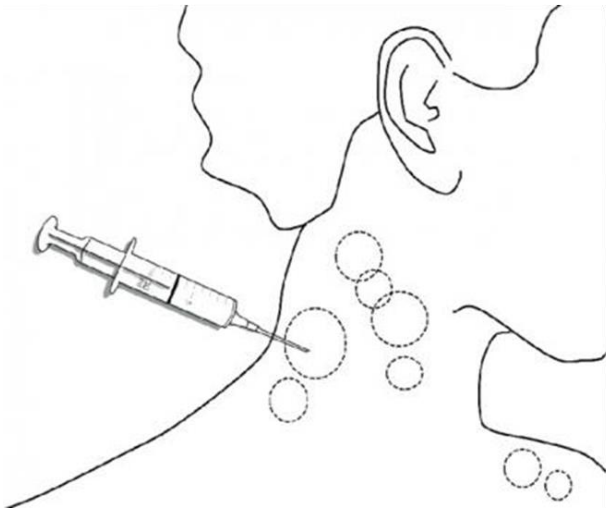
Two-dimensional fractionation may be carried out on more complex samples. This type of fractionation is typically accomplished using two orthogonal techniques, such as strong cation exchange (SCX) followed by reversed phase desalting. Stepwise elution from the SCX media may be carried out to partition the sample based on isoelectric point. These analyses may be done in packed pipet tips or by using functionalized magnetic beads. The use of robotics may help to increase throughput.

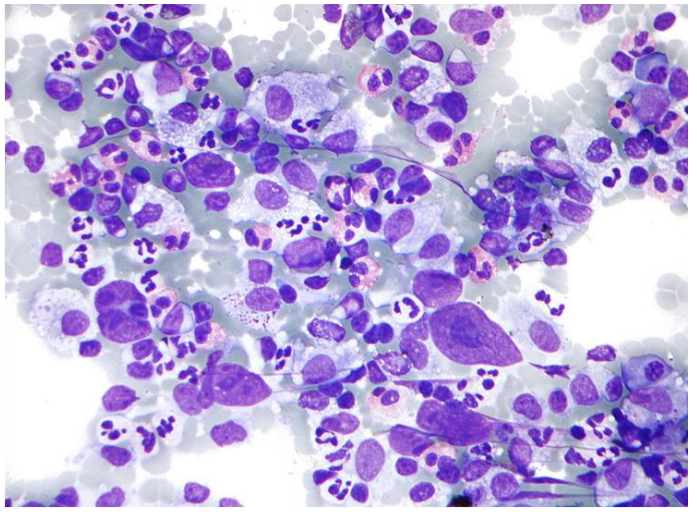




Cytology – Fine Needle Aspirates and Cytospins

Biopsies are sometimes taken by less invasive means such as fine needle aspiration or through scrapes or lavages. The collected cells are then cytospun onto a slide where they can be evaluated, traditionally through histological review, but also by mass spectrometry. The cells spun onto a slide can be prepared in the same manner as tissue sections and then imaged using MALDI or DESI. Histological staining can then be carried out on the sample after the mass spectral analysis and the results correlated with each other.





Cell Culture Analysis

Cell cultures are extremely important for preclinical studies. These samples can also be analyzed using MSI techniques. Larger cell pellets or 3D cell cultures can be frozen and sectioned as are traditional tissue specimens. These sections can be profiled or imaged and histologically stained to learn about environmental and treatment induced changes. Smaller or homogeneous cultures may be lysed using solvents and cleaned up using techniques applied to biofluids.