1216P A Spectroscopic Liquid Biopsy for the Earlier Detection of Multiple Cancers

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CONSIDERATIONS[1,2]

- Research into liquid biopsies is currently dominated by expensive and time-consuming circulating tumor DNA (ctDNA) and cell-free DNA (cfDNA) liquid biopsies.
- **Not all cancers and sub-types release genetic material**; there are generally only small amounts of early-stage ctDNA in a blood sample.
- Tumor derived signals are more abundant in late-stage cancer; for reliable detection of pre-cancer and early-stage cancer, **screening tests must also be sensitive to signals from non-tumor sources** (Figure 1).
- **Multi-omic Spectral Analysis (MOSA) enables a cost-effective, fast and easy-to-use blood serum-based liquid biopsy that could be the key solution to provide an early cancer detection tool.**

Figure 1. Non-tumor derived signals are stronger in earlier stages of the disease, whilst tumor derived ones are stronger in later stages

SAMPLES AND TECHNOLOGY[2,3]

- This multiple cancer discovery cohort contained **2092 patients**, including 1542 cancer samples (brain, breast, colorectal, kidney, lung, ovarian, pancreatic and prostate), and 550 non-cancer samples, which included a mixture of symptomatic (with non-malignant conditions) and asymptomatic patients (Figure 2).
- Patient serum samples were analyzed using the **Multi-omic Spectral Analysis (MOSA)** tool (Dxcover Ltd., Glasgow, UK) combining ATR-FTIR spectroscopy with machine learning algorithms to predict the presence of disease.[7]

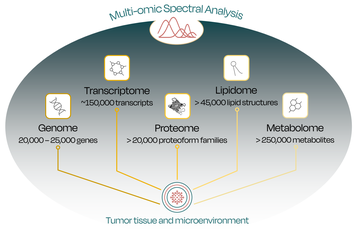

Figure 3. MOSA captures the phenotypic information of tumor tissue and microenvironment, such as the current -omics

- **MOSA can reach beyond ctDNA** and has proven to be inclusive of the whole spectrum of signals, including tumor molecules and non-tumor molecules released by the body during disease formation (i.e., early-stages; Figure 3).
- **The test only needs 9 µL of blood serum**, deposited onto a manufactured Sample Slide (Dxcover Ltd., Glasgow, UK) and dried for at least 10 minutes before spectroscopic collection.

Figure 2. Full patient cohort (n = 2092)

- The test consists of **infrared light interacting with the sample** and initiating molecular vibrations; this generates a distinctive signature that represents the whole biomolecular profile of the blood serum sample (Figure 4).

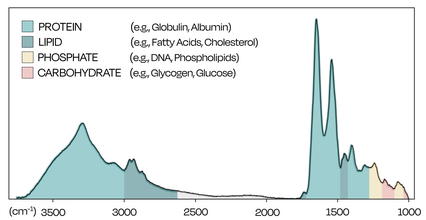

Figure 4. Infrared spectrum detailing the main blood serum components

MULTI-OMIC SPECTRAL ANALYSIS DETECTS CANCERS IN ASYMPTOMATIC AND SYMPTOMATIC POPULATIONS[3]

- This approach **can be fine-tuned to maximize either sensitivity or specificity depending on the requirements from different healthcare systems** and cancer diagnostic pathways (Table 1).
- The cancer v asymptomatic non-cancer (**C v NCA**) classification detected: **99% of stage I cancers at 58% specificity** (Fig. 5b); and **64% of stage I cancers at 99% specificity** (Fig. 5c).
- For cancer v all non-cancer (**C v NC**), the sensitivity-tuned model enabled: 90% sensitivity with 61% specificity (Fig. 5d); and **detection rates of 93% for stage I, 84% for stage II, 92% for stage III and 95% for stage IV** (Fig. 5e).

Table 1. MOSA can be tuned for high sensitivity or high specificity based on healthcare market requirements

Cancer type	AUROC	Sens (%) at 45% CV Spec	Spec (%) at 45% CV Sens
Brain	0.90	95	99
Breast	0.76	88	87
Colorectal	0.91	97	97
Kidney	0.91	99	96
Lung	0.91	100	95
Ovary	0.86	95	95
Pancreas	0.84	95	93
Prostate	0.86	93	96

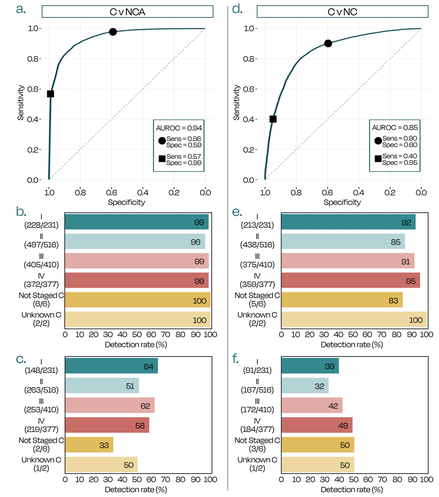

Figure 5. MOSA is highly sensitive in cancer detection within both asymptomatic (C v NCA) and symptomatic (C v NC) populations

Figure 6. MOSA detects differences between each individual cancer type; different cancers have different infrared signatures (NC, non-cancer; NCS, non-cancer symptomatic; NCS-F, NCS-females only; NCS-M, NCS-males only)

WGAN AUGMENTATION: THE CRC CASE[4]

- **Data augmentation** can be used to generate new data points to train deep learning models; Wasserstein Generative Adversarial Networks (WGANs) learn from real data to create new datapoints.
- Adding **WGAN augmented spectra is the only data augmentation method to produce a statistically significant improvement** when compared with augmenting with real spectra (Figure 7).
- This study investigated the ability of WGAN augmented spectra to improve the performance of a Convolutional Neural Network (CNN) to differentiate between CRC (n = 200) and symptomatic non-cancer (n = 459) samples.

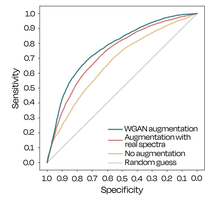

Figure 7. WGAN augmentation increases the AUROC compared to other or no data augmentation

Table 2. WGAN augmentation increases AUROC value of CRC classification

Dataset	AUROC
Train: 559-CRC dataset *Test*: 100-CRC dataset	0.91
Train: 559-CRC dataset + WGAN augmented spectra *Test*: 100-CRC dataset	0.96

- The results show that **WGAN augmented spectra can improve CNN performance**. When compared with a model that used no augmented spectra, adding WGAN augmented spectra to a CNN with the same architecture and same parameters, **increased the AUROC for the CRC dataset from 0.91 to 0.96** (Table 2).
- **Data augmentation could improve the overall model performance of the multi-cancer dataset**, as seen for the CRC case.

CONCLUSIONS

Multi-omic spectral analysis (MOSA) can:

- **Detect cancer earlier** with high sensitivity for stage I and II disease;
- **Fit seamlessly into current diagnostic pathways** due to a low integration barrier;
- **Offer the possibility of a combination approach with high specificity-based techniques** (e.g., NGS and metabolomics) to enable an effective multi-cancer early detection tool (Figure 8);
- Ultimately facilitate the liquid biopsies translational route to **improve prognosis and increase patient survival**.

Figure 8. A combination approach could facilitate early detection of cancer

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1. Liquid Biopsies
2. Serum Profiling
3. Multiple Cancers
4. WGAN

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