Prospective Evaluation of image-based Artificial intelligence Research and development tool for the identification of Biomarkers for Improved patient Outcomes (PEAR-BIO)

1 Abstract

Precision medicine has the potential to revolutionize cancer treatment and drastically improve outcomes. While genomic screening has become the gold standard for personalized cancer therapy, its predictive power is confined to select cancers and drug modalities, and is yet to show promise as a standalone drug selection tool for improving patient outcomes. For many therapies, genetic predictive biomarkers remain largely unknown. Additionally, genetic mutations alone may not be sufficient to elucidate the mechanisms whereby a therapy or a combination gives clinical survival benefits to a patient.

Pear Bio has developed an organ-on-a-chip technology and integrated computer vision pipeline to test various therapeutic regimens simultaneously using an individual patient's tumor. Initial development was performed on retrospective biobank samples across 8 solid tumor types. Ongoing observational clinical trials are aimed at establishing the tool's sensitivity and specificity in triple negative breast cancer (TNBC) in the neoadjuvant and metastatic settings, as well as validating the technology in renal, pancreatic, liver, brain and lung cancers.

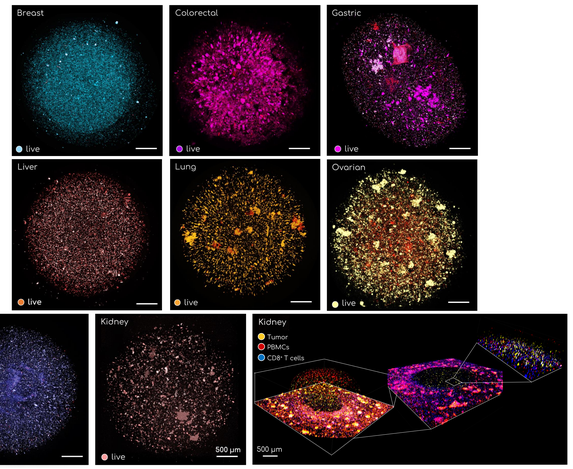

Figure 1. Physiologically-relevant 3D models across eight solid tumors - apoptotic cells NucView (red 528); scale bar 500 µm applies to all. Bottom right: Immuno-oncology 3D model of kidney tumor and matched immune cells (tumor, CellTracker541; PBMCs, CellTracker630; CD8+ T cells, CellTrace405).

For more detail about our workflow take a look at our presentation or come talk to us at ASCO booth #2114

2 Measuring patient outcomes *ex vivo*

Pear Bio uses proprietary hydrogel formulations to recapitulate the physiological tumor microenvironment and architecture *ex vivo* (Figure 1). Primary cells are cultured in multiple chips within a microfluidic device which allows drug dosing and clearing to mimic complex clinical regimens. Confocal live-cell imaging is performed over 4 days in our organ-on-a-chip while it is dosed with approved monotherapies and combination therapies in a microfluidic device. In TNBC, samples were dosed with doxorubicin (A) and cyclophosphamide (C) (1 day), followed by paclitaxel (T) with or without carboplatin (CarboTaxol) (2 days) at a high and low dose to recreate the chemotherapeutic AC-T and AC-CarboTaxol clinical regimens that the patients received (Figure 2-4).

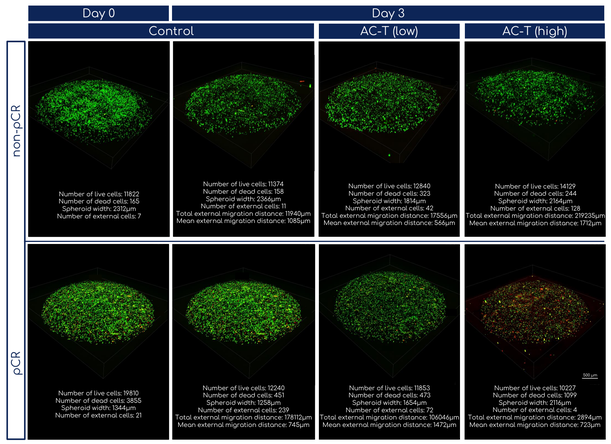

Figure 2. Representative confocal micrographs of non-pathological complete responder (non-pCR top) and pathological complete responder (pCR -bottom); live MitoView (green 488); dead NucView (red 528) at day 0 and 3 of treatment in Pear Bio's microfluidic device. Patient samples were treated with AC (1 day) followed by T (2 days) at high and low doses. Imaging was performed daily. Computer vision-extracted metrics for each chip are displayed below each image. Scale bar 500 µm applies to all.

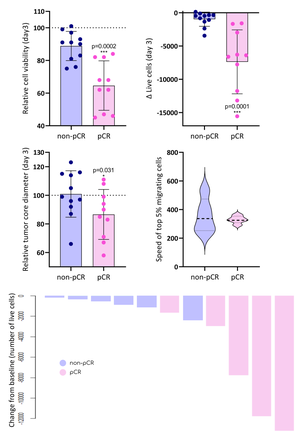

Figure 3. Quantification of cell behaviours via computer vision-extracted metrics across TNBC patients (n=4). Retrospective patient testing data is used to calculate tool's sensitivity and specificity in predicting pCR.

Treatments tested in the Pear Bio platform range from combination chemotherapy to targeted therapies such as PARP inhibitors and antibody-dug conjugates (Figure 4).

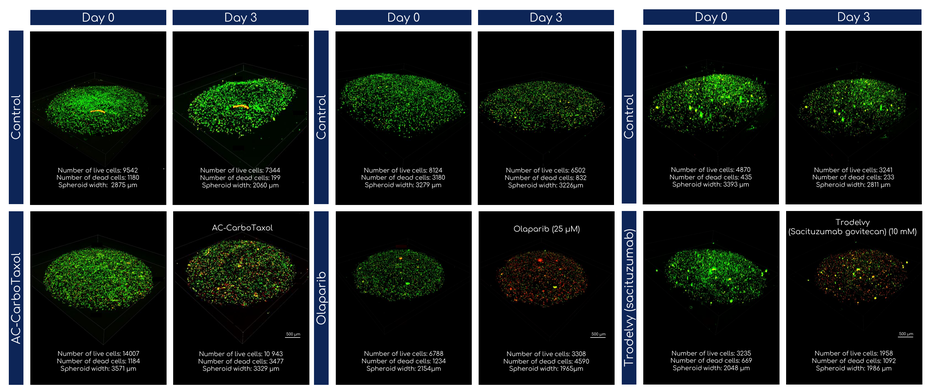

Figure 4. Representative confocal micrographs of triple-negative breast cancer patient samples treated with AC-CarboTaxol (with 1 day of doxorubicin (40 nM) and cyclophosphamide (50 µM) followed by 2 days of carboplatin (20 µM) and paclitaxel (20 nM)), Olaparib (25 µM) or Tradelvy (Sacituzumab govitecan, 10 mM) and control; live MitoView (green 488); dead NucView (red 528) at day 0 and day 3 of treatment in Pear Bio's microfluidic chips and device. Scale bar 500 µm apply to all.

3 Our patient cohort

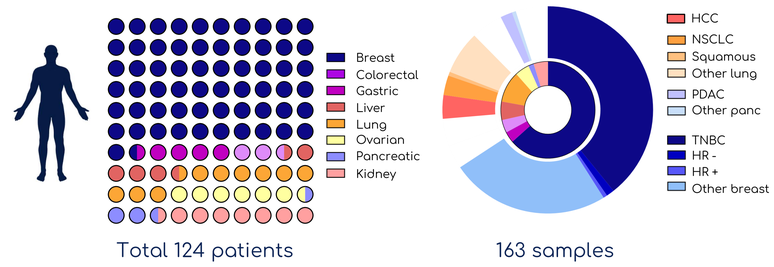

Figure 5. Pear Bio's patient cohort by cancer and subtype.

4 Predicting patient outcomes

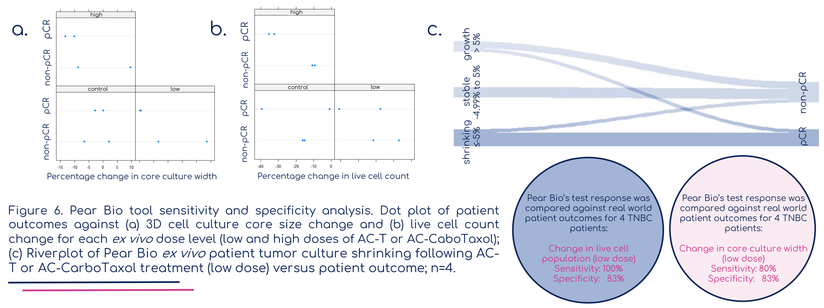

Figure 6. Pear Bio tool sensitivity and specificity analysis. Dot plot of patient outcomes against (a) 3D cell culture core size change and (b) live cell count change for each *ex vivo* dose level (low and high doses of AC-T or AC-CaboTaxol); (c) Riverplot of Pear Bio *ex vivo* patient tumor culture shrinking following AC-T or AC-CarboTaxol treatment (low dose) versus patient outcome; n=4.

5 Conclusions

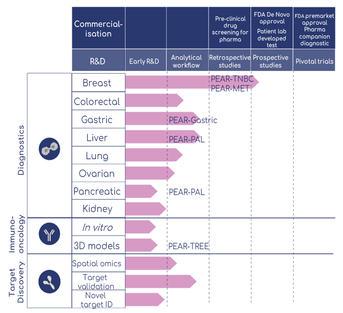

Figure 7. Pear Bio commercial, R&D and clinical trials timeline.

Pear Bio's technology was capable of predicting patient response with ≥80% sensitivity and specificity in a small cohort of TNBC patients. The technology has also been validated across 8 solid tumor types, where dissociated tumor cells show high viability in their physiologically relevant 3D microenvironments. Observational studies are planned in metastatic TNBC, liver, pancreatic, renal, brain and gastric cancers throughout 2022. Early R&D is progressing to include the testing of immunotherapies (immuno-oncology 3D models) and multi-omics studies.

6 Get in touch

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