Core needle biopsy – novel refinement technique

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Abstract

To fill the gap of adopting a translational tool to sample tumour specimens in mice, we assessed and validated this unique capability using a core needle biopsy (CNB) sampling method for preclinical tumour models.

Tumour sampling for diagnostic or research purposes was established in the clinic but not for preclinical cancer models.

CNB yields a large intact tissue fragment, therefore providing suitable samples for demanding pharmacodynamic (PD) endpoints such as imaging, proteomics and genomics.

Introduction

Identifying response biomarkers or drug resistance mechanisms preclinically requires the evaluation of tumours at baseline and during treatment.

Clinical methods for longitudinal tumour sampling, such as CNB, are difficult to scale down for mouse models.

Summary – materials and methods

This technique was applied in different tumour models but with preference in the Large Cell Lung Carcinoma (LCLC) as part of the project in interest. It was confirmed the sampling does not have any detrimental impact on the tumour growth kinetics or on Animal Welfare.

CNB samples were collected from cadavers using three different needle gauges to evaluate the sample yield.

This also prompted us to develop a pipeline to process relatively small biopsy samples for PD analysis by Western Blots, qPCR, WES/RNAseq, flow cytometry and histology.

Results

CNB procedure was adapted to sample mouse tumours (Figures 1 and 2).

Figure 1.

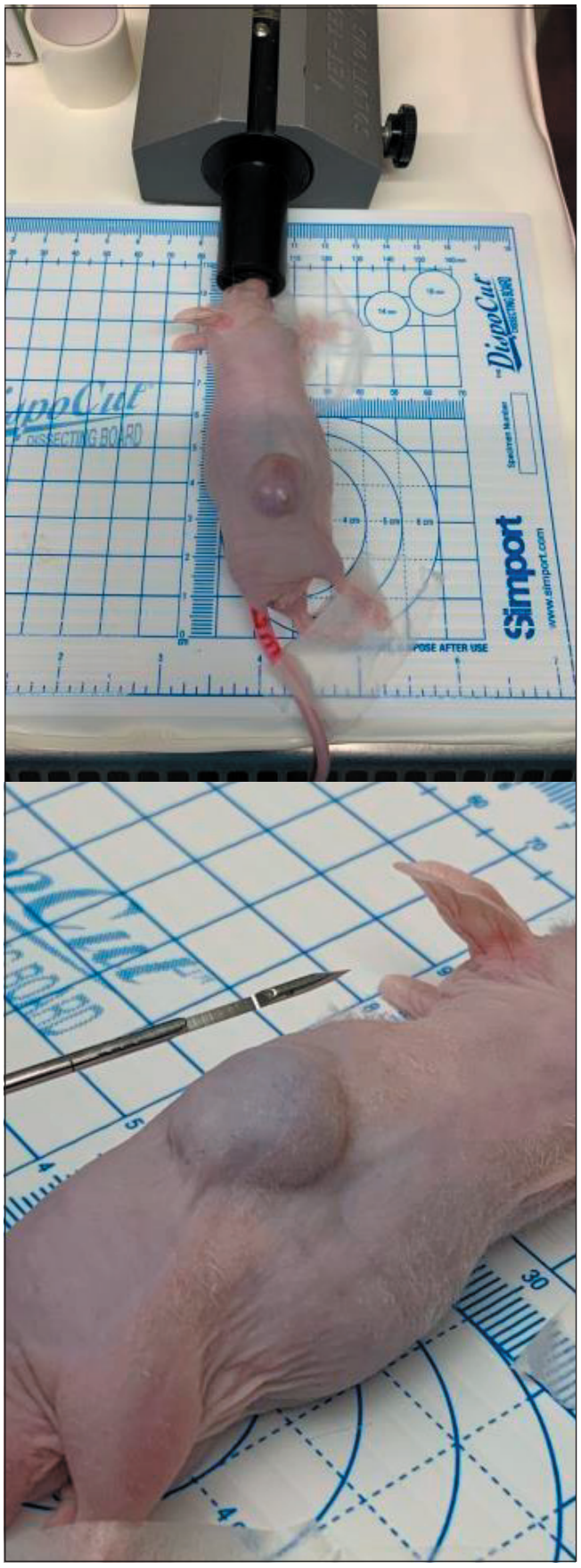

Figure 2.

CNB samples were collected from cadavers using three different needle gauges to evaluate sample yield.

16-gauge (g) needles were used to collect the best yield. This provided between 2 to 20 milligrams (mg) of intact tissue fragment (Figure 3).

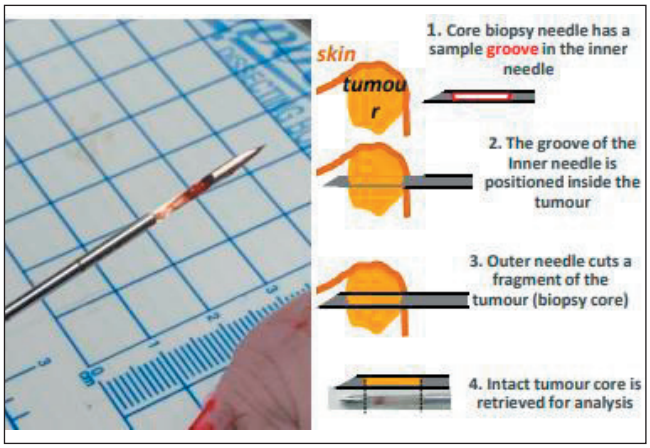

Figure 3. Biopsy sample (left), biopsy gun sampling modus operandi (right).

The data obtained demonstrated the CNB sampling technique did not compromise tumour growth. The mice recovered quickly and their bodyweight was not affected by the procedure (Figure 4).

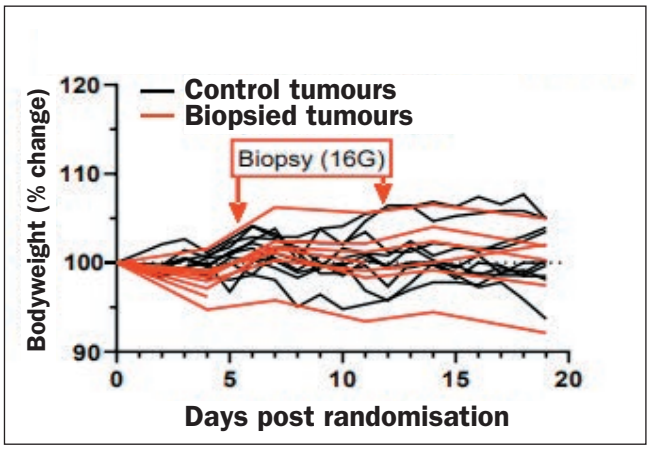

Figure 4. Bodyweight records during the length of the study with the CBN technique.

Advantages

- Biopsy sampling offers a non-terminal procedure for sample collection.
- CNB capability minimised biological variability within *in vivo* studies.
- This enabled longitudinal analysis of a treatment over time from efficacy studies, enabling simultaneous generation of pharmacokinetic (PK)/ pharmacodynamic (PD) and tumour growth inhibition (TGI).
- Check sustainability of a broad range of mouse tumour models for biopsy sampling.
- Reduces the number of animals required for preclinical studies (3Rs).

Next steps

- Optimise the procedure to maximise the success rate and increase the tissue yield in live animals.
- Check sustainability of a broad range of mouse tumour models for biopsy sampling.
- Conduct further studies utilising CNB sampling and then implement this method across other oncology projects.

Conclusion

Repeated tumour sampling using CNB enables a potential reduction of the number of animals required for an *in vivo* study while accelerating data and sample generation (e.g. running an efficacy and PK/PD in a single study.

CNB may be used to characterise heterogenous tumour responses (responders and non-responders) over the course of the study.

Pre-treatments biopsy may enable predictive biomarker assessment ahead of clinical trials.

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