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Repeated Ultrasound-Guided Liver Biopsies in Non-Human Primates

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Abstract

Despite improvements in serology, the need to collect a sample directly from an organ remains a valuable procedure in nonclinical research. The liver biopsy is an invasive procedure with potential risk for complications. Nonetheless, the procedure has been refined to become a rapid, precise, and safe collection method in non-human primates (NHPs), with a relatively short recovery period.

Ultrasound-guided non-terminal single liver collections have been successfully performed on 150 NHPs. Repeated non-terminal liver collections were performed on 198 NHPs with 2 or 3 biopsies (4 to 7 days apart), and on 37 NHPs with 6 to 9 monthly collections. In order to mitigate the risk associated with liver biopsies, a 2D ultrasound was used to identify major structures in and around the liver, to allow for the safe insertion of the biopsy needle (14 or 16G), and to monitor any potential bleeding post retraction of the needle. Minor complications such as prolonged recovery from sedation, second incision needed, or difficulty penetrating the hepatic capsule were noted for a handful of animals. These did not affect the health of the animals.

A monthly frequency has been shown to be successful for long-term studies requiring up to 9 liver biopsies per animal and no less than 4 to 7 days between occasions for up to 3 biopsies per animal. Based on these observations, ultrasound-guided liver biopsies have been proven to be minimally invasive, safe, and well tolerated in NHPs for non-terminal repeated collections.

Methods

The 2D ultrasound was selected as the most suitable approach for identifying major structures of the liver, allowing for a safe insertion of the biopsy needle (14 or 16G) and to monitor any potential complications post-surgery. This method offered a minimal level of stress for the animal, reduced the risk of complications, and allowed for a shorter post-surgery recovery period.

Each animal was anesthetized using a ketamine/xylazine mixture (13 mg/kg). Meloxicam (0.1 mg/kg), a nonsteroidal anti-inflammatory drug (NSAID), was administered to treat pain and inflammation associated with the surgical incision and the biopsy site, for three consecutive days.

The ultrasound was used to visually identify the liver and gallbladder during the insertion of the biopsy needle. An incision was made through the skin with a scalpel blade to provide access to an area of the liver, away from vital structures. A biopsy specimen was then collected from the right side of the liver.

The procedure consistently yielded a 1.5 cm length of useable liver tissue for analysis.

Results

A total of 385 NHPs underwent liver biopsy collections. Several factors determined how frequently a biopsy needed to be performed. The vast majority only needed a single collection, while some others required up to 9 collections over the span of 9 months. Within the scope of this evaluation, a total of 927 biopsy samples were collected across all animals.

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When the initial collection did not yield enough liver tissue, additional insertions of the needle were performed (data not presented).

Due to the relative position of some anatomical structures around the liver, a second surgical incision was occasionally required to access the liver from a different angle. This was required on 4 different occasions over 927 biopsies.

The most prevalent type of complication observed was an extended recovery time from sedation. In those cases, depending on the condition of the animal, an additional dose of atipamezole (reversal agent) was provided and/or subcutaneous or intravenous fluids were administered (saline or dextrose).

Type of Complications Encountered		
	N	%
Extra support required during recovery	13	1.4%
Second incision needed for collection	4	0.4%
Low sample size/Unable to collect a sample	4	0.4%
Total N. of biopsies	927	2.3%

Conclusion

Ultrasound-guided liver biopsies have proven to be a minimally invasive, well-tolerated and safe method for repeated biopsy collection from the liver in non-human primates.

Acknowledgments

B Knapp

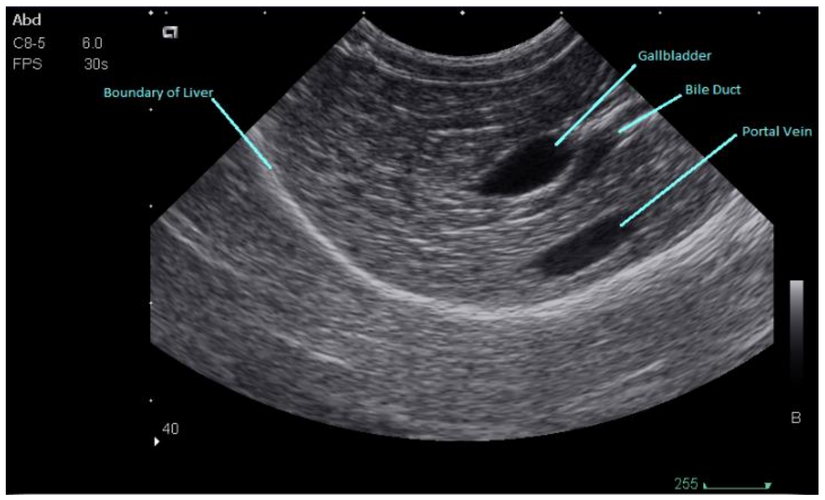

Figure 1. 2D ultrasound image of the liver (solid white line), gall bladder and large vasculature structures (black oval areas).

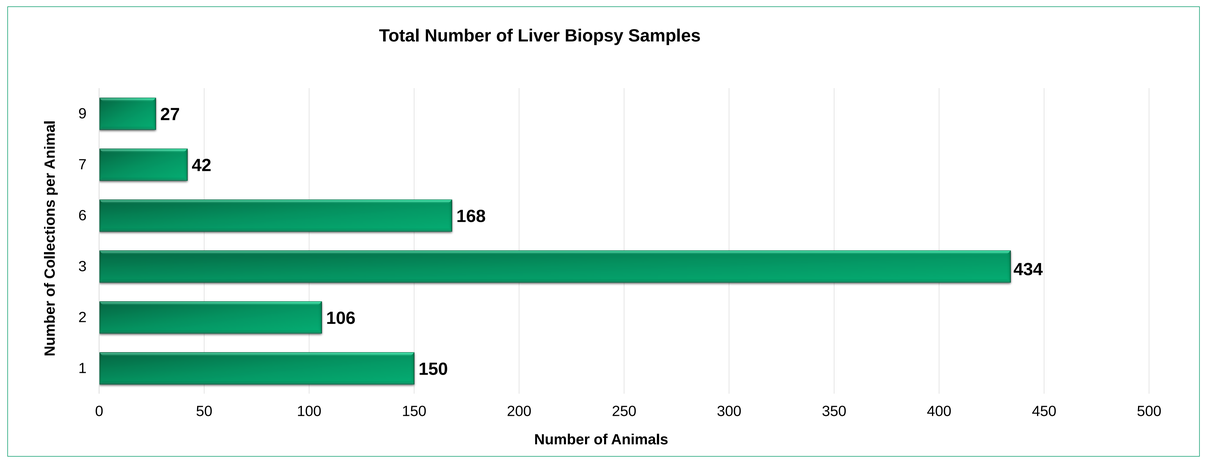

Figure 1. Total number of liver collections using a core biopsy needle over a maximum duration of 9 months