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Reducing gastrointestinal signal in mice for *in vivo* imaging with MPI

Background

Magnetic Particle Imaging (MPI) is sensitive enough to detect nanogram-levels of iron. Combined with low tissue attenuation, this sensitivity enables the quantitative detection of small populations of labeled cells. However, other sources of iron in the region of interest may contribute background signal, limiting the limit of detection and skewing quantitation. Some potential sources of iron are found in mouse feed and bedding, which, when ingested, contribute to gastrointestinal (GI) signal observed in *in vivo* images.

GI signal is problematic for several reasons. First, high signal from the gut may conceal MPI-tracer signal from nearby regions of interest, limiting detection. Second, GI signal unintentionally included in the quantification of the region of interest will lead to an overestimation of the amount of iron. For these reasons, this study examined fasting, choice of bedding, and laxatives as methods to mitigate unwanted GI signal in mice for in vivo imaging.

Experimental Set-up

NOD SCID gamma mice (bred at Robarts Research Institute) were fasted overnight for 12h in cages with only water. All other cage elements were removed except bedding, which was retained on the recommendation of animal care services. Since fasted mice tend to ingest their bedding, two types of bedding were compared, cotton and corn. Four fasting conditions were tested (n = 1 per condition): (i) cotton bedding without laxative (ii) cotton bedding with laxative (iii) corn bedding without laxative and (iv) corn bedding with laxative. One tablet of chocolate laxative was left in the cage for conditions (ii) and (iv).

MPI data was acquired using a 2D high sensitivity setting (3.0 T/m gradient, 20 mT (X-channel) and 26 mT (Z-channel) excitation. The imaging parameters were: FOV = 12 x 6 x 6 cm, 1 average and acquisition time of 2.8 minutes. Total MPI signal was quantified by setting a threshold to capture signal above 5 times the standard deviation of background noise. Samples of mouse feed, corn and cotton bedding were imaged in plastic tubes. Images of mice were acquired immediately prior to fasting and again after 12 hours of fasting. After fasting and imaging, mice were returned to fully restored cages.

Results

Conventional mouse feed and bedding produce MPI signal (Figure 1). The MPI signal was approximately ten times higher for cotton bedding compared to corn. Fasting led to a reduction in MPI signal from GI region in all mice (Figure 2). MPI signal was reduced by 36% when mice were fasted in cages with cotton bedding and by 86% when mice were fasted in cages with corn bedding. The use of laxatives in addition to fasting had little effect – reducing GI signal by 35% with cotton bedding and 79% with corn bedding.

Conclusion

Fasting is an effective way to reduce the unwanted signal from the GI tract. During fasting mice tend to ingest their bedding. Corn bedding produces much less MPI signal than cotton bedding. Providing corn bedding for fasting mice had the largest reduction in GI signal. The addition of laxatives did little to further reduce the MPI signal.

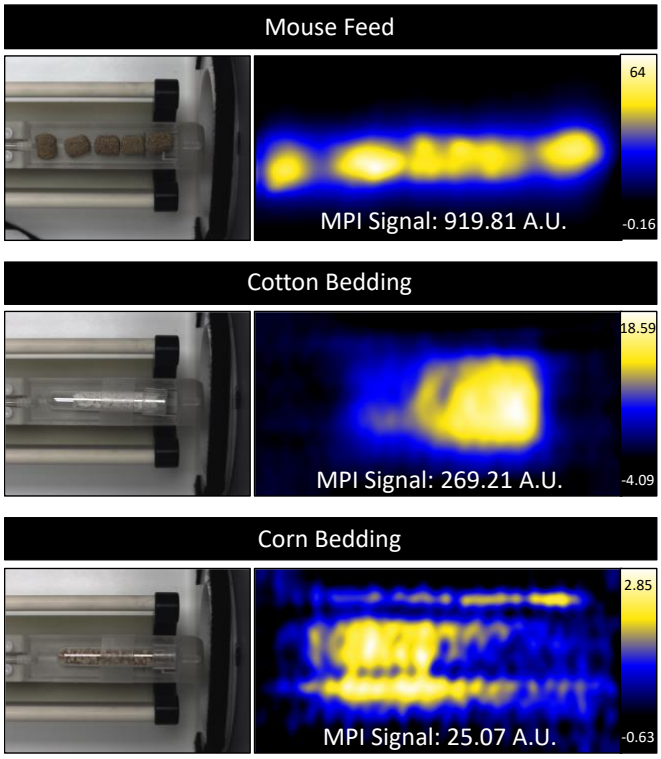
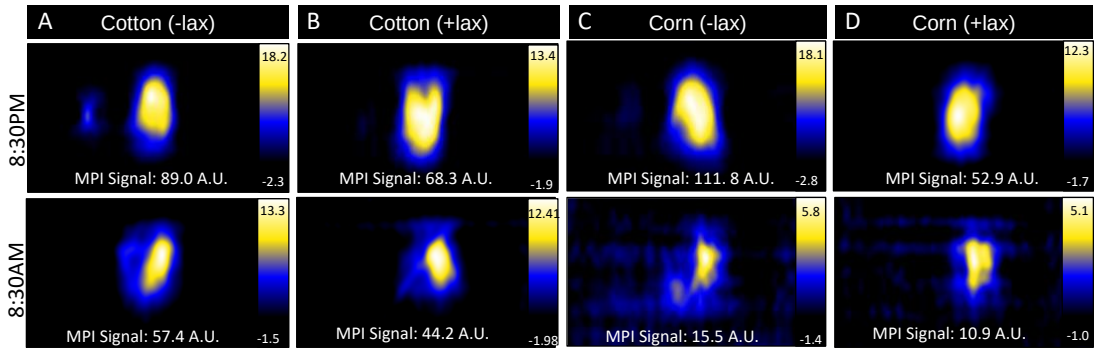


Figure 1: MPI of samples of mouse feed and different types of bedding used in mouse cages. Mouse feed and bedding produce MPI signal. Cotton bedding had a much higher MPI signal compared to corn.



No Laxative – GI Signal (A.U.)		
	Cotton	Corn
Before fasting	89.01	111. 81
After fasting	57.38	15.47
	Reduced signal by 36%	**Reduced signal by 86%**

With Laxative – GI Signal (A.U.)		
	Cotton	Corn
Before fasting	68.33	52.91
After fasting	44.24	10.94
	Reduced signal by 35%	**Reduced signal by 79%**

Figure 2: MPI of mice fasted for 12 hours using either cotton or corn bedding, with and without laxatives. Gastrointestinal (GI) MPI signal was reduced after fasting in all mice (N=1 per condition). Mice in cages with corn bedding had a lower GI signal compared to cotton bedding post-fast. Laxatives did not appear to impact GI signal.