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In vivo vs. *ex vivo* magnetic resonance imaging in mice

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A commentary on

Wanted dead or alive? The tradeoff between in vivo vs. ex vivo MR brain imaging in the mouse
by Lerch, J. P., Gazdzinski, L., Germann, J., Sled, J. G., Henkelman, R. M., and Nieman, B. J. (2012). Front. Neuroinform. 6:6. doi: 10.3389/fninf.2012.00006

The use of high-resolution MRI for the evaluation of structural changes in the mouse brain is rapidly gaining favor with researchers. The decision to use either *in vivo* or *ex vivo* imaging is often a practical one. For example, technical limitations, such as the availability of appropriate equipment to image *in vivo*, may force an investigator to use *ex vivo* imaging. Conversely, animal availability may limit the number of samples used at each time-point in an *ex vivo* experimental design, but not affect an *in vivo* design. But what if we were not limited by these considerations? What if we could decide which approach to take based entirely on which approach would yield the best data?

In "Wanted dead or alive? The tradeoff between *in vivo* vs. *ex vivo* MR brain imaging in the mouse" presented by Lerch et al. (2012), this is exactly what is considered. *Ex vivo* imaging benefits from greater resolution and sensitivity due to the lack of constraints on imaging time, the use of tighter fitting coils, high concentration contrast agents, and a lack of movement artifacts. *In vivo* imaging allows for the longitudinal analysis of structural change, a benefit that can not be underestimated. Longitudinal studies lend themselves to other forms of statistical analysis, such as repeated measures ANOVAs, which can increase the statistical power of the studies. But beyond the obvious differences, how sensitive are these MRI measures to structural changes on the order of 5% of the total volume of a neuroanatomical structure? The authors describe a series of statistical analyses (based on imaging data they acquired) used to evaluate the tradeoffs between the use of *in vivo* (longitudinal) analysis and *ex vivo* (cross sectional) analysis.

For a remarkably complex problem, the results are surprisingly straightforward. Firstly, *ex vivo* imaging is more precise than *in vivo* imaging. In cases where precise time-course data is not required, *ex vivo* imaging provides better results. This is due to the lower within subject variability inherent to *ex vivo* imaging (higher resolution, no movement). However, if changes in absolute volumes or rates of change are required, *in vivo* imaging provides better information. Interestingly, in longitudinal experiments, the addition of more subjects, rather than more time-points, increases statistical power more rapidly.

Secondly, the kind of analysis used matters. Spatial normalization to an unbiased consensus average, correcting for gross differences in brain size, decreases the population standard deviation markedly (by approximately 50%). Before spatial normalization, population standard deviations are about the same size as the effects to be observed. Clearly, spatial normalization is a crucial step in any form of volumetry.

As *in vivo* imaging equipment and expertise become more common, the decision between the use of *in vivo* or *ex vivo* imaging begins to boil down to choosing the best tool for the job; *ex vivo* for precision, *in vivo* for time-course, and spatial normalization for all.

REFERENCE

Lerch, J. P., Gazdzinski, L., Germann, J., Sled, J. G., Henkelman, R. M., and Nieman, B. J. (2012). Wanted dead or alive? The tradeoff between in-vivo versus ex-vivo MR brain imaging in the mouse. *Front. Neuroinform.* 6:6. doi: 10.3389/fninf.2012.00006

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