Quantitative Magnetic Resonance: A New Noninvasive Way to Assess Body Composition in Pets

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Introduction

Obesity and weight management in dogs and cats are growing concerns in veterinary medicine and the companion animal nutrition industry. The ability to accurately, safely and rapidly obtain *in vivo* body composition measurements in animals is critical in health and nutrition studies, as well as in the clinic, to monitor patient progress in response to a weight-loss program or diet change. A multitude of methods and techniques exists for the assessment of body composition and/or body condition in pets that can range from simple field methods to complex laboratory methods, and each method/technique has its own inherent advantages and disadvantages. This review will focus on the recent research and method validation of a newly emerging technology called quantitative magnetic resonance (QMR).

Glossary of Abbreviations

BCS: Body Condition Score
BIA: Bioelectrical Impedance Analysis
BIS: Bioelectrical Impedance Spectroscopy
CT: Computed Tomography
DEXA: Dual-Energy X-ray Absorptiometry
FFM: Fat Free Mass
FM: Fat Mass
LBM: Lean Body Mass
MRI: Magnetic Resonance Imagery
TBW: Total Body Water
QMR: Quantitative Magnetic Resonance

Models for Body Composition

Currently, the most common model applied to studies to assess body composition is the two-compartment (2-C) model that partitions the body into either fat mass (FM) or fat-free mass (FFM) compartments. The FFM compartment of the 2-C model collectively consists of water, protein, carbohydrates, and minerals. However, this model has the inherent limitation that FFM is assumed to remain constant in composition, particularly regarding water content, and composition is the same among individuals. Measurement of total body water (TBW) is the primary strategy to derive the FFM, but this assumes that hydration of FFM is constant. Tracer-dilution methods using tritiated water (^3H_2O), deuterium water (D_2O or ^2H_2O), or doubly labelled water ($^2H_2{}^{18}O$)[3] are the "gold standard" for quantifying TBW and, by extension, FFM. By contrast, and most typically in human research, a 4-compartment (4-C) model goes further to validate new technologies or methodologies as the accepted reference method to assess body composition.[3,4] The 4-C model separately measures body mass, bone mineral mass (typically assessed by dual-energy X-ray absorptiometry [DEXA]), TBW mass (typically assessed by D_2O), and body volume to control for biological variability in both TBW and bone mineral mass.[3,4] To date, the 4-C model has not been used in body composition methods in companion animals.

Methodologies for Assessing Body Composition in Cats and Dogs

In routine veterinary practice, clinicians tend to rely on a subjective assessment of body condition using a body condition score (BCS) system, such as the 9-point BCS system,[5,6] to support feeding recommendations to pet owners. More recently, morphometric measures have been evaluated to establish models of predicting body composition in overweight and obese cats and dogs, which also show utility in a clinical setting.[7,8] Although clinically useful, these methods are only semi-quantitative.

In research, objective measures of *in vivo* body composition are essential, and thus are obtained via DEXA or D_2O dilution. These two technologies have been used in studies with dogs[9-11] and cats,[9] and were originally validated for accuracy against direct whole-body analysis as the "gold" standard. In recent years, D_2O has been widely relied upon as the reference standard in the evaluation and validation of new methods and techniques for animal studies, including cats and dogs. Other methods also have been studied compared to DEXA as the reference method, including morphometric measures,[12,13] ultrasonography[13] and bioelectrical impedance analysis (BIA),[13] as well as ultrasonography versus direct whole-body analysis.[14] Newer methods such as QMR,[15,16] bioelectrical impedance spectroscopy (BIS),[17,18] and computed tomography (CT)[19,20] have demonstrated distinct advantages yet possess certain limitations and challenges.

QMR Technology Overview

Functionally, QMR is a technology that uses hydrogen (proton) nuclear magnetic resonance principles. The response of a hydrogen proton is determined by its chemical bonding; thus, total hydrogen protons associated with any lipid molecule is a measure of fat mass, which behaves differently than the hydrogen protons in lean tissue. More specifically, nuclear magnetic resonance instruments for composition analysis create contrast between soft tissues by taking advantage of the differences in relaxation times of the hydrogen proton spins in different environments. Radio pulses cause proton spins to precess and emit radio signals that are then received and analyzed. The amplitude, duration and spatial distribution of these signals are related to properties of the material scanned. The high contrast between fat, muscle tissue and free water is further enhanced by application of uniquely composed radio pulse sequences. Therefore, QMR can specifically distinguish lean tissue mass from fat tissue mass with the distinct advantage of being able to obtain accurate measurements while the animal is awake and free moving within a confined space. Since the technology is capable of measuring free water and TBW, intra-day changes in body water related to hydration status become feasible, and importantly, the technology is not dependent on the subject's hydration status when measuring lean or FM.

In contrast to the use of DEXA, CT or magnetic resonance imaging (MRI) that require an animal to be sedated to prevent movement, the QMR technology can obtain rapid, accurate and numerous measurements within a day while the dog or cat is awake. This is particularly beneficial for animals considered to be at greater health risks for sedation, including extremely young, geriatric or sick animals. The requirement for sedation often limits routine use of DEXA, CT or MRI for healthy and adult animals. Compared to standard MRI, QMR has no contrast agent or acoustic noise and the level of radio frequency heating is about a million times lower. This would suggest that there are minimal to no hazardous effects of QMR (personal communication from GZ Taicher, EchoMRI). Therefore, the potential exists to use QMR to examine total body water, FFM and FM in health-sensitive pet populations. Table 1 provides a comparison of advantages and disadvantages of QMR and alternative methodologies as they relate to use in cat and dog studies.

QMR Validation of Body Composition Data in Cats and Dogs

Since the first QMR study[21] to measure TBW and body composition of lean and fat mass was reported, QMR has been validated for use in many different species, including dogs,[12] cats,[13] mice,[22,23] rats,[23-2] pigs,[26,27] humans,[28-30] and chickens.[31] Direct whole-body analysis was used to validate QMR in mice, rats, chickens, and pigs, whereas D_2O dilution was used for cats, dogs and humans. All have revealed that values for TBW, lean body mass (LBM) and fat mass are highly correlated (r^2 = 0.80 to 0.98) to results generated by the reference method. These validation studies also have revealed that the QMR method has high precision (CV<2%) for measurement of fat mass, LBM and TBW.

Awake Versus Sedated Data Collection: One of the key attributes to the QMR technology is the ability to obtain body composition measurements while the animal is awake and unrestrained. A Plexiglas (polymethylmethacrylate) crate, which allows the pet to sit or lie down during the scan, fits

Table 1. Summary of advantages and disadvantages of various body composition methodologies utilized and validated for cats and dogs.

Method	Single Scan or Measurement Data	Animal Sedation Typical	Equipment Cost	Data Analysis Difficulty	Multiple Daily Measures**	Safety Risk
D_2O	hours	No	moderate† low††	moderate	No	none
QMR	<3 min	No	high	easy	Yes	low to none
DEXA	10-15 min	Yes	high	moderate	No	moderate
CT	1-15 min	Yes	high	high	No	moderate
MRI	20-60 min	Yes	high	high	No	moderate
Ultrasonography	<5 min	Yes	moderate	high	Yes	low
BIA/BIS	1-2 sec	Yes	low to moderate	easy	Yes	none
BCS	5 sec	No	none	easy	Yes	none
Morphometry	<2 min	No	none	easy	Yes	none

* low=$10-$10,000; moderate=$10,000-$100,000; high=>$100,000
† based on cost of the mass spectrometry equipment
†† based on cost of per sample analysis if run by analytical laboratory with established equipment and isotope quantification protocols
¶ easy=minimal training required to collect data; moderate=some level of expert training to routinely collect accurate data; high=significant expertise for device operation and/or data/image analysis
** multiple daily measures would be possible with multiple daily sedations

in the measurement chamber of the QMR. Validation studies with dogs[12] and cats[13] confirmed that QMR measurements of TBW, FFM and FM did not significantly differ whether the pet was awake or sedated. Specifically, these measures differed by only 2.0%, 2.2% and 4.3%, respectively, for dogs, or 3.9%, 3.4%, and 4.0%, respectively, for cats. It is important to note that this data was representative of a single QMR scan while awake or sedated. Protocol refinement in cats demonstrated that performing in-triplicate scans reduces the difference considerably between awake and sedated states to 0.2%, 2.0%, and 0.2%, respectively, thus improved the confidence of collecting QMR data in awake animals. However, this increases the total scan time per animal from approximately 3 min to 10 min.

QMR Measurement Accuracy in Cats and Dogs: Similar to most other body composition methods or technologies, review of the QMR-based literature indicated that QMR technology underestimates or overestimates FM, TBW and/or FFM compared with results for the reference methods. In addition, the relative accuracy differs substantially by species (Table 2). In most QMR validation studies, TBW was over- or underestimated by less than 6.4%. However, in dogs, QMR underestimated absolute TBW by 10.2%, yet results were highly correlated (r=0.96) to the reference method. FFM determination was similar to that of TBW. The determination of FM by QMR is most variable among species, as some studies reveal a high level of accuracy (rat, piglet and human females), whereas considerable differences compared to reference methods were observed in others (mouse, chicken, dog, cat, and human male, Table 2). In all species, the validation studies demonstrated that the QMR and reference method measurements were highly correlated (r^2>0.80), which allows for the generation of species-specific correction equations for TBW, FFM and FM by linear regression analysis to facilitate an accurate calculation of each measure (Table 3).

QMR in Lean-Mass Hydration Assessment of Cats and Dogs: Unique to QMR is the ability to calculate the FFM hydration constant for an individual animal. The hydration constant associated with FFM is generally considered to be 73.2%,[32,33] and this average proportion has been reported in cats and dogs as well.[9] Although there is relative stability of average FFM hydration among species supporting the wide use of 73%,[32] considerable individual variation has been reported in humans (n=9; 68-81%),[32] as well as in dogs and cats (n=16, 6 dogs and 10 cats; 59.4-88.4%).[9] In another study,[10] investigators reported a similar, but slightly lower, mean FFM hydration constant in 75 lean and overweight dogs at 71.3%.

The QMR technology can overcome the use of an assumed FFM hydration and provide a determination for each cat or dog. The FFM hydration constant can be effectively calculated from data acquired via QMR with TBW and FFM measurements. In a population of 58 beagles with BCS from 3 to 8, average "corrected" FFM hydration was 72.3%,[15] but individual variation ranged from a minimum of 69.2% to a maximum of 75.8%. Also, in two separate cat populations, 16 different FFM hydration averages were reported as 72.2% (trial 1; min/max: 66.9-77.2%) for 58 cats with BCS from 3 to 8 and 68.4% (trial 2; min/max: 63.2-72.7%) for 32 cats with BCS from 3 to 9.

The ability to simultaneously and accurately measure TBW and the FFM hydration might provide insight on the hydration status or at least influence the assumptions used to determine components of body composition of an animal, particularly in overweight animals. Although it is not surprising that the TBW proportion would decrease with increasing obesity because of an increased proportion of body fat, it was unexpected to find that FFM hydration decreased as the percentage of body fat increased in dogs.[15] In addition, a study in humans found that the LBM hydration constant increases with age, but this was driven by a decrease in LBM as TBW

Table 2. Summary of validation studies examining measurement accuracy (overestimation or underestimation) using the quantitative magnetic resonance method relative to the reference method in several different animal species.

Animal	TBW	FM	FFM	Reference Method	Citation
Dog	↓10.2%	↓15.4%	↓13.4%	D_2O	15
Cat	↓1.4%	↓29.0%	↓4.4%	D_2O	16
Rat	↓5.5%	↑5.0%	↓12.5%	Whole-body analysis	24
Mouse	ND	↑29.0%	↓7.8%	Whole-body analysis	22
Chicken	↑4.0%	↑34.0%	↓1.1%	Whole-body analysis	31
Piglet	↓6.4%	↑2.0%	↓3.6%	Whole-body analysis	26
	↓3.1%	↑4.1%	↑2.1%		27
Human	ND	↓11.1% males	ND	D_2O	30
	ND	↑3.5% females	ND	D_2O	30

TBW= total body water ↓=underestimated relative to reference method
FM=fat mass ↑=overestimated relative to reference method
FFM=fat free mass ND=not determined

Table 3. Correction equations for TBW, lean body mass and fat mass prediction for QMR (scan obtained with the dog or cat awake but with minimal movement) on the basis of results for the D_2O dilution method.

			Cross-Validation*		
Dependent Variable	Regression Equation	Model r^2	Difference (kg)	Difference (%)	References
TBW					
canine	$(1.1506 \cdot QMR_{TBW\ [in\ kg]}) + 0.2104$	0.923†	−0.06 ± 0.05	4.4 ± 0.4	15
feline	$(1.0674 \cdot QMR_{TBW\ [in\ kg]}) - 0.1156$	0.841†	2.28 ± 0.06	5.5 ± 0.7	16
Lean body mass					
canine	$(1.1659 \cdot QMR_{lean\ body\ mass\ [in\ kg]}) + 0.088$	0.931†	−0.08 ± 0.06	4.0 ± 0.4	15
feline	$1.074 \cdot QMR_{lean\ body\ mass\ [in\ kg]}) - 0.076$	0.864	3.11 ± 0.08	4.5 ± 0.7	16
Fat mass					
canine	$(0.9844 \cdot QMR_{fat\ mass\ [in\ kg]}) + 0.3526$	0.890†	0.10 ± 0.05	14.8 ± 2.2	15
feline	$(0.9541 \cdot QMR_{fat\ mass\ [in\ kg]}) + 0.2713$	0.892	0.83 ± 0.07	18.8 ± 3.6	16

*Mean ± SE values for the absolute difference and the percentage difference between predicted and actual measurements for the D_2O dilution method. †Value of the model. r^2 was significant ($p<0.001$).

remained unchanged.[34] In the future, studies involving overweight or obese geriatric populations for both companion animals and humans might need to examine the FFM hydration and potential impact on overall hydration and nutritional status.

Finally, FFM hydration has biological importance that is also applicable to growth, sex, body size, and acute or chronic illnesses.[32] Recent work in 16 Labrador Retriever puppies demonstrated that QMR can be used to observe the developmental reduction of FFM hydration from 89.7% at birth to 76.9% at 8 weeks of age (Spears J, Zanghi B, unpublished data). Not only does the QMR FFM hydration reveal that the assumption of 73.2% may need to be used with caution in studies of overweight or obese populations of animals, particularly dogs, but also that a safe technology exists to regularly monitor the early development transition of lean mass water content in very young animals.

Summary

The QMR technique is readily applicable to animal nutrition and body composition studies, with distinct advantages compared with the use of DEXA and D_2O dilution. Perhaps its greatest advantage is that it eliminates the need for sedation or anesthesia of subjects, and thus is completely non-invasive. The greater precision of QMR (CV, 2%), compared with DEXA (CV, 6%[9]), implies that QMR will be a valuable technique for assessment of weight management in individual animals on a longitudinal basis. Although BCS determined by experienced people is a convenient and practical estimate of body composition, it is semi-quantitative and subjective in nature. By contrast, QMR provides a relatively rapid (<3min/scan) and reliable quantitative measure that eliminates the subjectivity of BCS assessment among observers.

Combined, these positive attributes contribute to a considerable advantage in the ability to frequently assess body composition changes during nutrition studies and in veterinary medical patients. It also is possible to eliminate health concerns and decreased food intake associated with anesthesia, particularly in extremely young or old animals in which the health risks are greater.

Although the initial acquisition cost of the device is substantial, the investment in a technology like QMR can allow veterinarians in referral practices and universities and animal nutritionists to safely and more routinely assess loss of adiposity, as well as evaluate maintenance of lean mass following various intervention strategies. This would be particularly beneficial in aged or diseased pets that are underweight or overweight without the risks of anesthesia and provides a promising advancement in healthy weight loss and weight-management studies or aging studies.

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