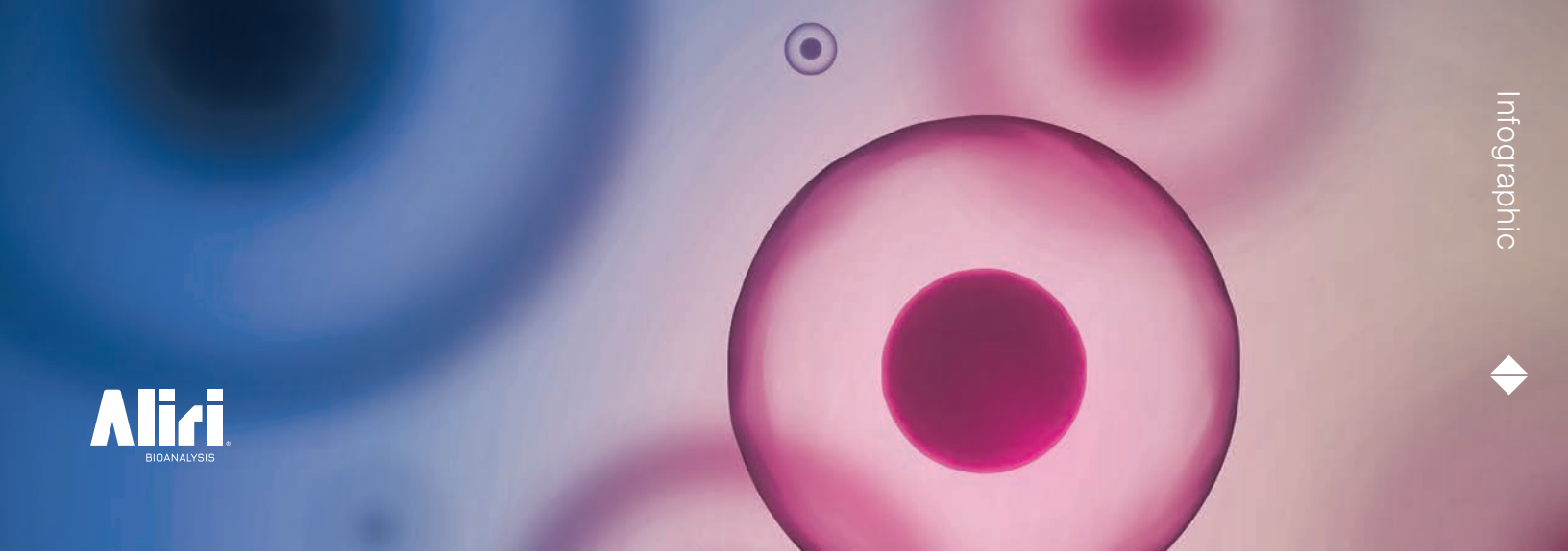

Infographic

When to use quantitative mass spectrometry imaging (QMSI) instead of quantitative whole-body autoradiography (QWBA)

With differing benefits and disadvantages—and price tags that make the right choice essential—understanding when to choose one technology over the other (or when to combine them) can make or break the timeline and budget for a burgeoning biopharmaceutical company.

WHAT IS QUANTITATIVE MASS SPECTROMETRY IMAGING (QMSI)?

QMSI offers label-free biodistribution of analytes simultaneously after preclinical test subject or clinical sample collection. Whole-body samples or tissues can be used, and they require rapid freezing and sectioning. Thin sections are analyzed using mass spectrometry and digitally imaged to detect drugs, metabolites and any other biomolecules or analytes of interest. The use of isolated tissues or whole-body samples enables analysis of drug distribution and concentration directly at the site of action. When performed with samples collected from different times post-exposure to the drug of interest, QMSI can be used to establish PK parameters and metabolism in target tissues.

KEY ADVANTAGES	KEY DISADVANTAGES
Label-free quantification of thousands of analytes	Sensitivity is “molecule-dependent”
Excellent differentiation among parent drugs, metabolites, and other substances	Requires development of an analytical method
Highly specific in quantification by location in tissue	Not validated by the regulatory agencies as an alternative to QWBA
Used in preclinical (early and late stages) and clinical studies	
Frequently used on isolated organs/biopsies and on rodent whole bodies	

WHAT IS QUANTITATIVE WHOLE-BODY AUTORADIOGRAPHY (QWBA)?

QWBA involves use of a radioactive substance administered to a preclinical test subject prior to euthanasia or extraction. Samples are then rapidly frozen and embedded for sectioning. Thin slices are imaged to detect the radio-labeled signal. The use of whole tissues or whole-body samples enables analysis of the radioactive signal distribution and concentration without differentiating the drug from the related metabolites. When performed with samples collected from different times post-exposure to the drug of interest, QWBA can be used to establish drug clearance and metabolism in target tissues.

KEY ADVANTAGES

- Highly precise quantification capabilities, even at low and high limits of detection
- Spatial resolution at the cellular level
- Gold standard technique for late-stage regulatory distribution studies

KEY DISADVANTAGES

- No specificity: impossible to differentiate the drug from the related metabolites
- Mainly used on whole-body tissues at a late preclinical stage
- Requires investment in a radiolabeled drug product (time-consuming and costly)

KEY FEATURES

	QMSI	QWBA
APPLICATIONS	Preclinical and clinical quantification, differentiation, and drug distribution and metabolism studies	Preclinical drug distribution studies, dosimetry, metabolism, and clearance studies
DRUG DISTRIBUTION	Yes	Total signal drug + metabolites
SENSITIVITY	Molecule-dependent	Highly sensitive and linear
SPECIFICITY	Excellent differentiation of parent drug and metabolites	Impossible to discriminate the drug from the metabolites
LABELING	Label-free	Radiolabeling
PRECISION/ ACCURACY	Molecule-dependent	High if the radiolabeling is
PREPARATION	Tissue snap-freezing, sectioning and analytical method preparation (e.g. matrix deposition for use of a MALDI ion source)	Molecule radiolabeling process, tissue snap-freezing and sectioning Requires radiation shielding for health and safety considerations
SAMPLE EFFICIENCY	High	High
TEST DURATION AFTER PREPARATION	Rapid (minutes to hours)	Moderate (days to weeks) due to the radiolabeling process
COMBINED PROCESSES FOR INCREASED UTILITY	Matrix-assisted laser desorption/ionization (MALDI), QWBA, laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS), imaging mass cytometry, and LC-MS/MS	Radiolabeled mass balance, plasma pharmacokinetic studies, QMSI, and LC-MS/MS

WHEN TO USE QMSI VERSUS QWBA

Both techniques require highly trained staff, meticulous sample preparation, and expert analysis.

QMSI allows you to de-risk the time and investment in a drug candidate at some early preclinical stage of drug development by:

- Confirming the dose selection and the mode of administration at an early stage based on the drug biodistribution
- Confirming that the drug can reach the site of action (organs and/or histological regions)
- Anticipating safety concerns by identifying any unexpected accumulation (drug and/or metabolites) in specific organs or histological regions
- Identifying and/or studying the metabolites distribution compared to the drug to understand the metabolic process of the drug candidate

Quantitative autoradiography remains the gold standard technique at the late stage for the regulatory agencies. However, QMSI is frequently used in support of the autoradiography if the radiolabeled results are unexpected due to:

- The need to discriminate the drug from the metabolites signal
- A problem or a doubt in the radiolabeling process of the drug candidate

Consider the following when selecting one method or a combination of methods for your drug program:

De-risk your drug candidate choice at an early stage	✓ QMSI
Precise quantification in overall tissue is essential	✓ QMSI
Precise differentiation between drug and metabolites is essential	✓ QMSI
Biodistribution regulatory submission at a preclinical late stage	✓ Autoradiography

Speak to an expert to ensure you're taking the right approach for quantification and distribution studies.

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