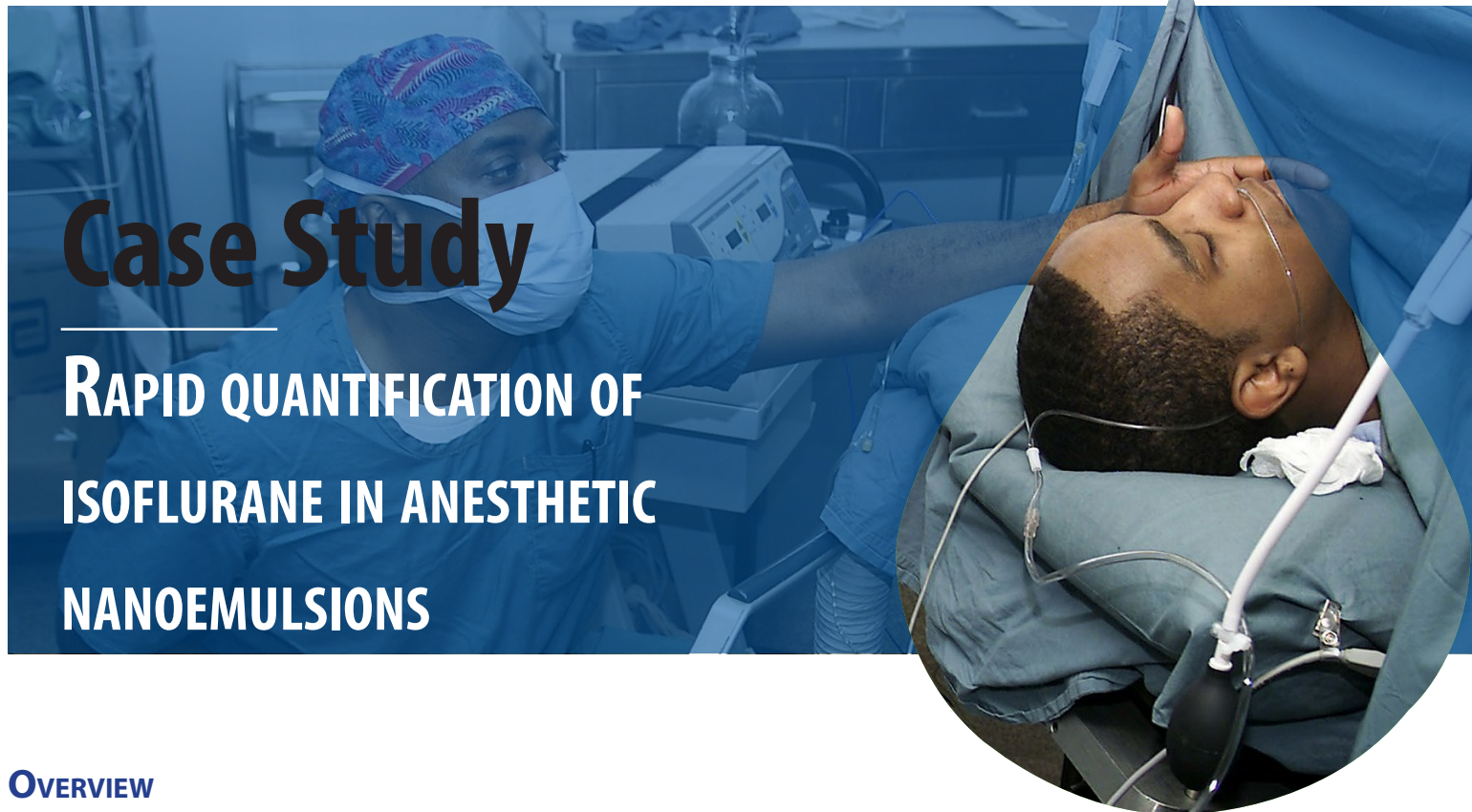


Case Study

RAPID QUANTIFICATION OF ISOFLURANE IN ANESTHETIC NANOEMULSIONS



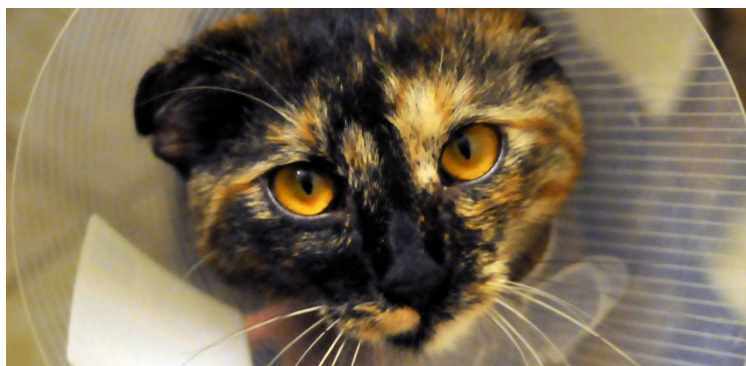
OVERVIEW

Because of an increase in the number of outpatient surgeries, and a decrease in insurance reimbursements, there is a significant need to develop new technologies in the field of anesthesia with improved patient safety, faster induction and emergence, and a reduction in the requirement of personnel and costly machinery.

In the last few years, emulsions of halogenated ethers have emerged as a technology with potential as both induction and maintenance agents. Stable emulsions are attractive formulations for a variety of drugs due to enhanced drug solubility or due to the new mechanism of drug delivery. There is an increased interest in intravenously administrable emulsified halogenated ether

Volatile Anesthetics (fVA) acting as general anesthetics as well as protective agents through ischemic pre and post-conditioning. The emulsification of halogenated ethers is a key since their direct injection proved to be dangerous in early studies.

An example of such fVA is isoflurane, usually administered via inhalation, however, causing airway irritation. Emulsification of isoflurane allows a different drug delivery mechanism as well as reduces the evaporation of this volatile drug. The escape of volatile anesthetic in operating room would present a potential hazard to surgical staff.



“ We were using a different high-shear processor, but just could not get enough particles through the sterile filter. With just a few passes through the ShearJet processor, we had particles in the 150-160 nm range which easily passed through the 200 nm sterile filter. This is what we needed for safety.

Lead Project Researcher

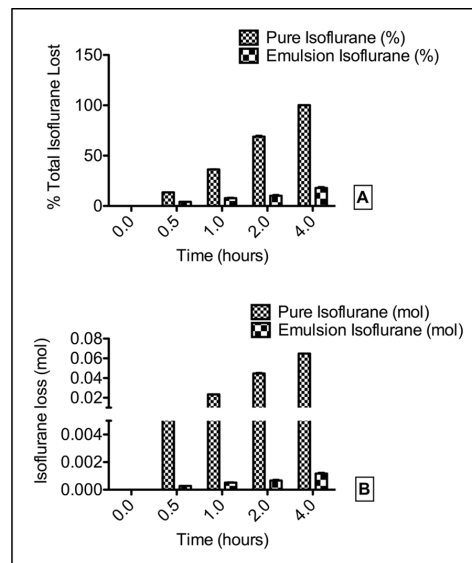
RESULTS

The evaluation of evaporative isoflurane loss from 10 mL beakers containing 2 mL of either pure isoflurane or emulsified isoflurane. Graph B represents loss in terms of total molecules lost and in Graph A as percent of total isoflurane lost relative to T = 0. The emulsion was made with standard formulation concentrations (10 % v/v perfluorocarbon and isoflurane, 2 % w/v surfactant).

The coarse emulsion was processed on a Dyhydromatics ShearJet HL60 in 5 distinct passes at 15,000-16,000 PSI and then was diluted with a final 1/3 volume of saline solution. Nanoemulsion particle size was determined by dynamic light scattering. All manufactured emulsions used in the study were between 150-160 nm.

In this study, the research team describe the successful development and testing of a rapid Attenuated Total Reflectance Fourier Transform Infrared Spectroscopy (ATR-FTIR) method for determination of isoflurane content in anesthetic nanoemulsions. Due to the slower evaporation rate, these nanoemulsions have a higher safety rate relative to pure isoflurane. The isoflurane content

Graph A
Isoflurane lost



Graph B
Molecules lost

measurement obtained with the ATR-FTIR method are accurate and in agreement with measurements obtained with the standardly used HPLC. Moreover, the ATR-FTIR method proved to be 20 times faster and has therefore the potential to lower drug development costs in this formulation and other hydrophobic pharmaceutical nanoemulsions.

CHALLENGES

- 1 Polypharmacy
- 2 Drug solubility
- 3 Evaporation during manufacture

SOLUTIONS

- 1 Create intravenous drug
- 2 Perfluorocarbon (oil in water emulsion – optimizes delivery) comes off blood in microseconds
- 3 Emulsified isoflurane evaporates more slowly

FUTURE PLANS

There has been tremendous success in the veterinary field trials with animal induction in 30 seconds (with just one injectable drug), and awake and fully ambulating within ten minutes. We hope to expand in veterinary medicine and move into human trials with initial results showing patients awake and fully ambulating within 15-17 minutes simply by ventilating the patient.



The ShearJet HL60 electric hydraulic processor runs sample sizes as small as 3mLs in distinct passes or continuous runs. The easy to use touch screen display puts simplicity at your fingertips, displaying relevant information in real time.