

Design and Performance Improvement of an Ion Cooling Cell for a Quadrupole Mass Spectrometer

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ABSTRACT

Previously, simulation results have demonstrated the concept and optimization of the cooling cell for an enhanced resolution and sensitivity triple quadrupole mass spectrometer (QMS). In this study an improved version was fabricated and implemented in a QMS for performance evaluations. Necessary design changes have been made, including to the quadrupoles, resistive components, and electrostatic lens, in order to overcome engineering and gas dynamic constraints. The primary goal of this cooling cell development is to reduce the kinetic energy (K.E.) of ions of all masses with minimal ion loss.[1]

INTRODUCTION

A QMS is capable of detecting spatially ion information patterned by a multipole mass filter.[2] The performance of this instrument can be detrimentally affected by incoming ion beams that require conditioning prior to mass analysis. Among many existing schemes, buffer-gas cooling is of great interest as it stabilizes the ion beam effectively. The ion cooling technique discussed here introduces a cooling gas, e.g., nitrogen or helium, to efficiently cool down ions to the temperature of the background gas. Collisional cooling of ions and inert gas atoms or molecules in a RF-driven quadrupole that provides a strong confining force results in a compact ion beam with narrow K.E. distribution at the exit of the cooling cell.

INSTRUMENTATION

This version of the ion cooling device consists primarily of a quadrupole ion guide having two pairs of wire-wound rods, and a metal gas enclosure with gas restrictors and electrostatic lenses at two ends which contains helium cooling gas. (Figure 1) An RF voltage at 2.7MHz is applied to the quadrupole with opposite phases of the voltage for radial confinement. A DC gradient along the ion drift path is created by resistive wire-wound rods with different DC potential at two ends. This field facilitates ion transfer through dense cooling gas.

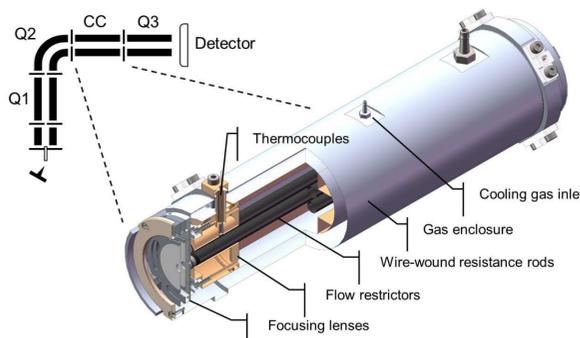


Figure 1. Thermo Scientific™ TSQ Quantiva™ Triple-Stage Quadrupole Mass Spectrometer equipped with a Gen IV cooling cell for ion K.E. control.

Note that the inscribed radius (r_0) of the Gen IV cooling cell quadrupole is extended from 1.45 to 3.05 mm, resulting in greater ion acceptance at the cell entrance while still maintaining acceptable RF radial confinement. (Table 1)

Table 1. Specifications of cooling cell generations

	Gen III	Gen IV
Rod Dimensions	Φ3.18, L 226.3 mm	Φ5.98, L 222.3 mm
r_0	1.45 mm	3.05 mm
Resistance	5Ω	317Ω
Conductance Limit	Φ1 mm	Φ4 mm

New resistive rods have been fabricated using specific resistance wire securely crimped onto the electric insulated rods. [3] When a potential difference is applied across the resistive path, it forms a linear superposition of a DC gradient and existing RF field along the instrument direction.

The presence of a DC current and RF power on resistive conductors induces temperature rise that may cause material expansion and possible short circuits. A thermal conductance test was conducted to ensure a functional resistor quadrupole in high temperature environment. A rod temperature of 58C was measured with a reasonable axial field (0.9 V/cm, 5 Watts), and the temperature of 85C was measured in a stress test that utilizes a 1.35 V/cm drag field (13 Watts) on the rods. (Figure 2) No sign of mechanical failures was found during all tests at ambient.

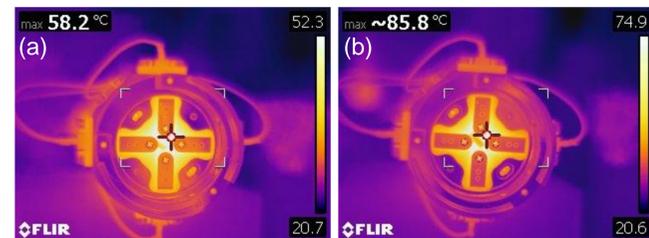


Figure 2. Resistive temperature rise of the cooling cell measured by a thermal imaging camera. Temperature measurements are done when a (a) 20 V and (b) 33 V DC gradient applied on the rods.

In the previous design, poor heat dissipation of the resistive rods overheated the soldered joint, which compromised the axial drag field, particularly for high mass ion scans. The current design utilizing wire-wound resistors allows reliable connections that prevented mechanical failures from occurring during daily operation. Resistance drifts in the range of 320-325 Ohm were measured in the stress test when temperature increased to 85C. No change in the DC field is expected as the voltage distribution on the resistive wires remains the same along the rods.

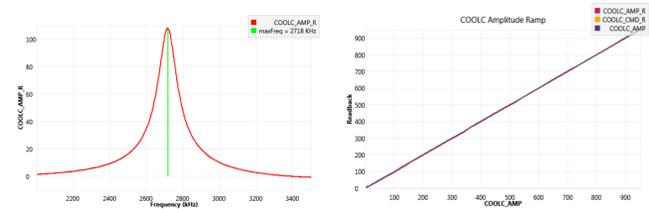


Figure 3. RF frequency dipping and ramping results indicate a functioning cooling cell quadrupole.

Note that the required DC gradient is typically below 10 V_{DC}. RF frequency swiping and voltage ramping by a high DC gradient show normal responses, indicating no connection issue during the operation. (Figure 3)

MATERIALS AND METHODS

Sample Preparation

Thermo Scientific™ Pierce™ triple quadrupole calibration solutions, Extended Mass Range and polytyrosine-1,3,6, are used for the instrument tuning. Alprazolam (MW 308.77) at concentrations from 1.5 femtogram to 5 picogram was prepared using the solution of 20/80 HPLC-grade quantitative experiments.

Test Method(s)

To evaluate the system performance, a Thermo Scientific™ Vanquish™ UHPLC system was coupled to the MS to measure linear dynamic ranges for various operation modes. Solvents used in the UHPLC system consisted of 2 mM ammonium formate and 0.1% formic acid in water (mobile phase A) and methanol (mobile phase B). Five ul. of the solution for each concentration are loaded into the analytical column at a flow rate of 300 uL/min. The LC-SRM separation used a curve gradient of 5% B in 0.5 min, 5%-40% in 0.7 min, 40-80% in 1.9 min, and 95% in 2.4 min.

Data Analysis

Customized triple quadrupole tune instrument control software was developed for MS operations. LC operation, data acquisition and data analysis were performed using Thermo Scientific™ Xcalibur™ 4.1.50 Software.

RESULTS

Cooling Effect

The effect of ion cooling was observed by sweeping the quadrupole RF amplitude. Initially, without the cooling gas, dramatic oscillations of the ion intensity were found with cooling cell RF amplitude varied in the range of 0-850V_{Q-P}. The oscillations were mitigated by introducing a small amount of helium to the cell, suggesting the stabilization of the ion trajectories by the helium buffer. (Figure 4)

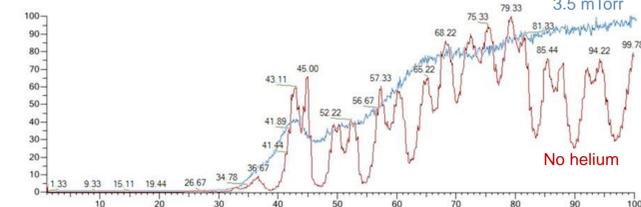


Figure 4. Ion intensity responses of polytyrosin-3 (m/z 508) as the function of RF amplitude with no cooling gas (Red) and 3.5 mTorr helium (Blue)

Transmission Improvement

Electrostatic lens stacks with 2, 4, 4 mm diameter apertures were initially placed at the two ends of the cell for device coupling and flow conductance purposes. The small aperture conductance limit next to the quadrupole appeared to reduce transmission, in particular for high mass ions. (Figure 6a) The analyzer chamber pressure increased linearly with the cooling cell pressure and quickly exceeded the upper operation limit when a 4,4,4 mm aperture lens set was used. (Figure 5). In view of this result, a 2 mm conductance limit that maintains the chamber pressure within the operation limit was deemed necessary.

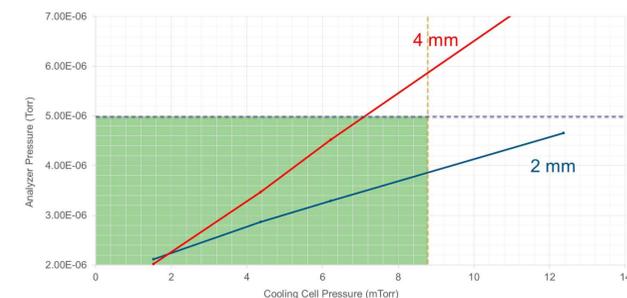


Figure 5. The pressure variation in analyzer chamber as the function of the cooling cell pressure for 2 and 4 mm aperture conductance limits.

Based on the simulation results, the original lens configuration may cause ion loss at the post-acceleration lens. The spectra of polytyrosin-1,3,6 supports the simulation showing low ion abundance at high mass. (Figure 6b) Instead of using a small aperture at the post-acceleration lens position, we moved it to the focusing lens position, resulting in the highest transmission and less mass discrimination. Simulation results have shown that a 4 mm post-acceleration and 2 mm focusing lens combination provides reasonable focusing at the cell entrance/exit, facilitating better overall transmission. The lens switching produced improvements in the high/low mass ratio (Figure 6c and 6d) as well as ion abundances of all masses.

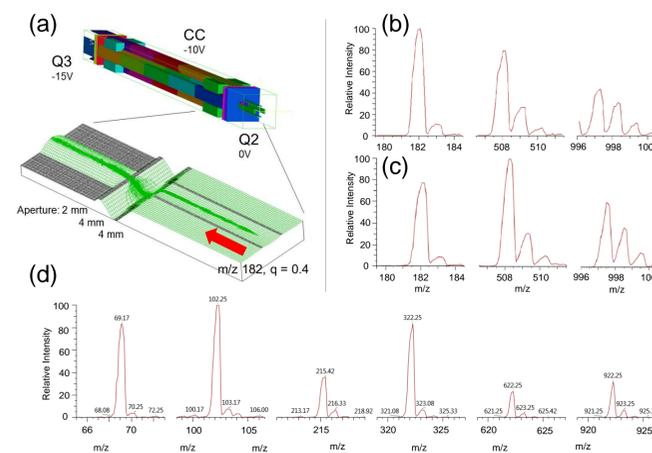


Figure 6. (a) Ion simulations of the cooling cell optics and polytyrosin-1,3,5 spectra for (b) original and (c) modified lens configuration. (d) EMRS spectrum using modified lens configuration.

As shown in Figure 7, a 450 ag alprazolam injection can be detected by the presented LC-MS system equipped with a cooling cell. The LC flow rate was set at 300 uL/min and the MS system was operated in SRM mode with unit resolution (FWHM 0.7) and 1 sec dwell time. The source parameters are set as follows: spray voltage, 3000 V; capillary temperature, 350C; vaporizer temperature, 375C; and collision gas pressure, 1.5 mTorr.

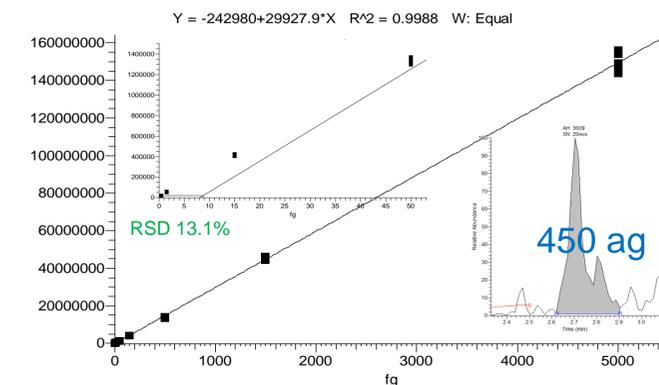


Figure 7. A calibration curve shows LOQ and linear dynamic range of the LC-TSQ system with cooling cell.

CONCLUSIONS

- The redesigned cooling cell shows better thermal stability and better quadrupole functionality as compared to the previous generation.
- The wire-wound resistor quadrupole design provides better mechanical robustness and allows generation of a higher axial field, if needed.
- Simulation and experimental results show better transmission by the new lens set arrangement. The performance of the MS system was demonstrated. Sub-femtogram quantitation of alprazolam was achieved by the improvement on the new cooling cell lens configuration.

REFERENCES

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ACKNOWLEDGMENTS

The authors thank Nick Izgarian for his useful input and technical support relating to construction of the resistive quadrupole.

TRADEMARKS/LICENSES

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