



PRESENCE OF 3,4-METHYLENEDIOXY-N,N-DIMETHYL AMPHETAMINE (MDDM) IN A FATAL MDMA-OVERDOSE

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Case history and Introduction

- 31-year-old man

- ✓ Found dead at home next to his bed
- ✓ Post-mortem interval of ± 7 days: advanced state of putrefaction
- ✓ No external signs of injury
- ✓ Known alcohol abuse problem

Death caused
by drugs of abuse ?



■ Screening of available fluids and tissues

- ✓ Amphetamine / methylene-dioxyamphetamine designer drugs ???
- ✓ LC-MS/MS [1]: ESI+ Q-TOF hybrid mass spectrometer (Micromass)

✓ Results:

- Massive MDMA overdose:

e.g. [MDMA]_{femoral blood}: 13.5 µg/mL

- A “strange” peak in the EIC: m/z 208.10 to m/z 105+133+135+163

T_R 17.5 min

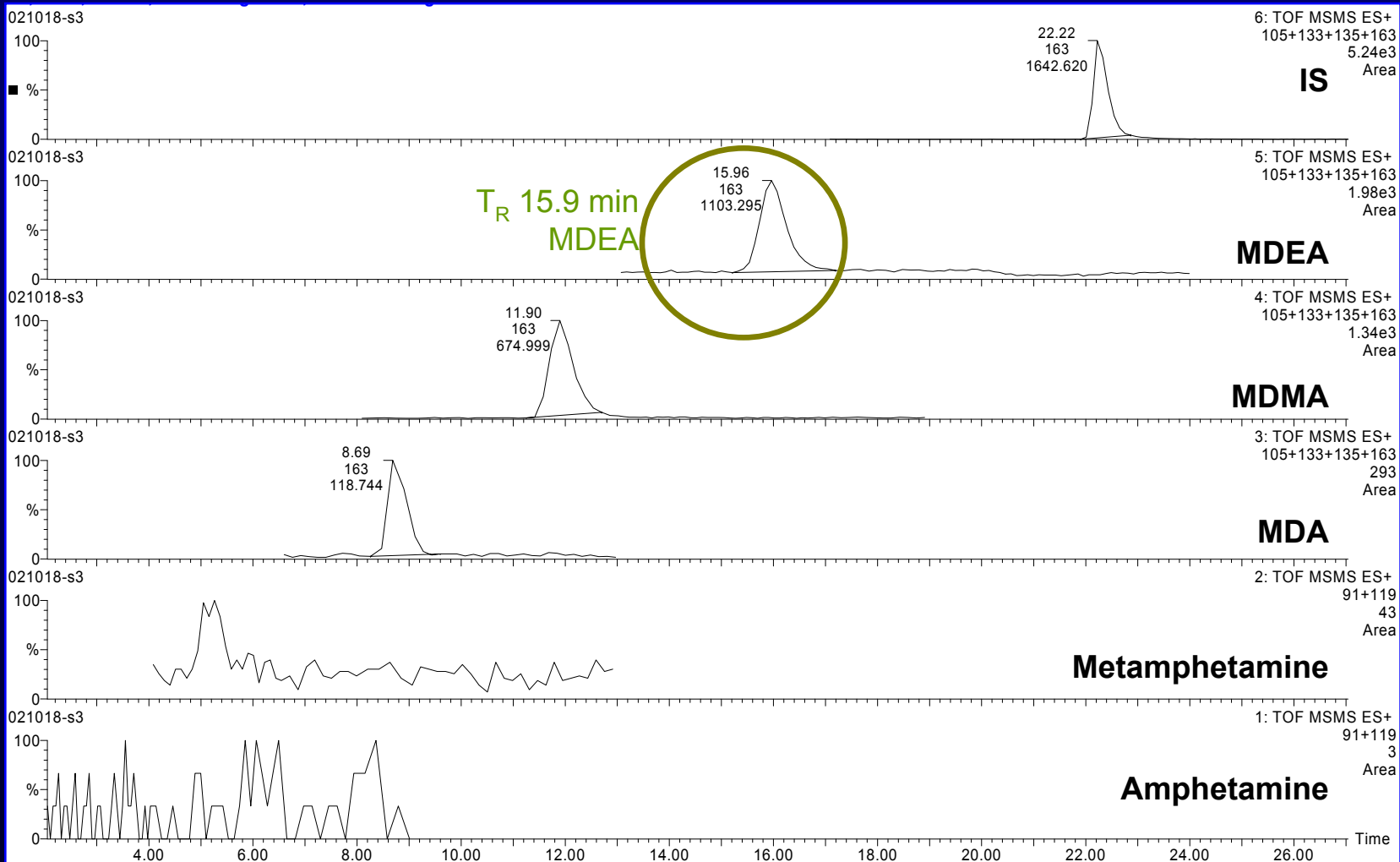
- MH^+ , transitions = MDEA
- $T_R \neq$ MDEA (T_R 15.5 min)



Unidentified
substance

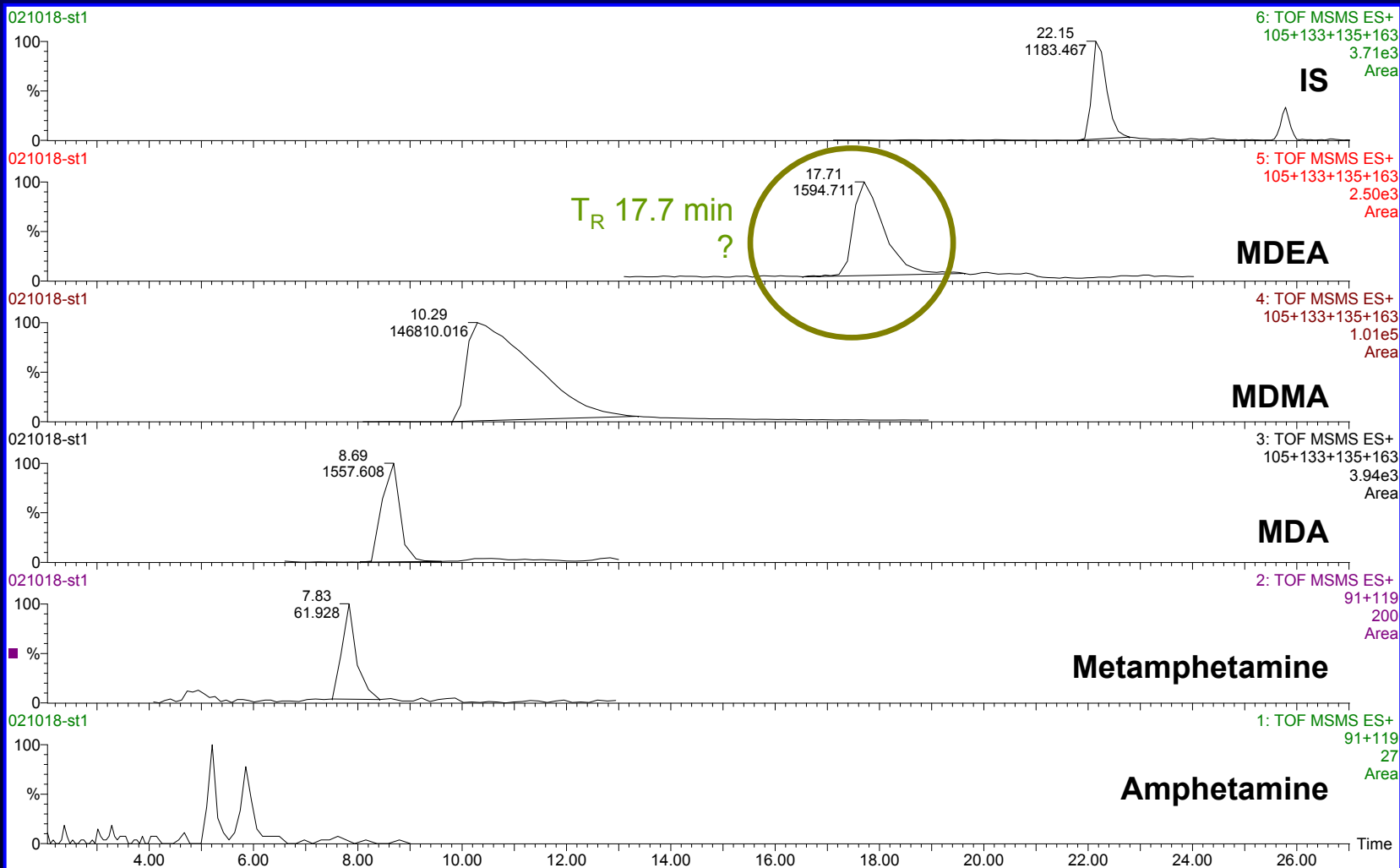


[1] K Mortier et al, J Chrom B 779 (2002) 321-330



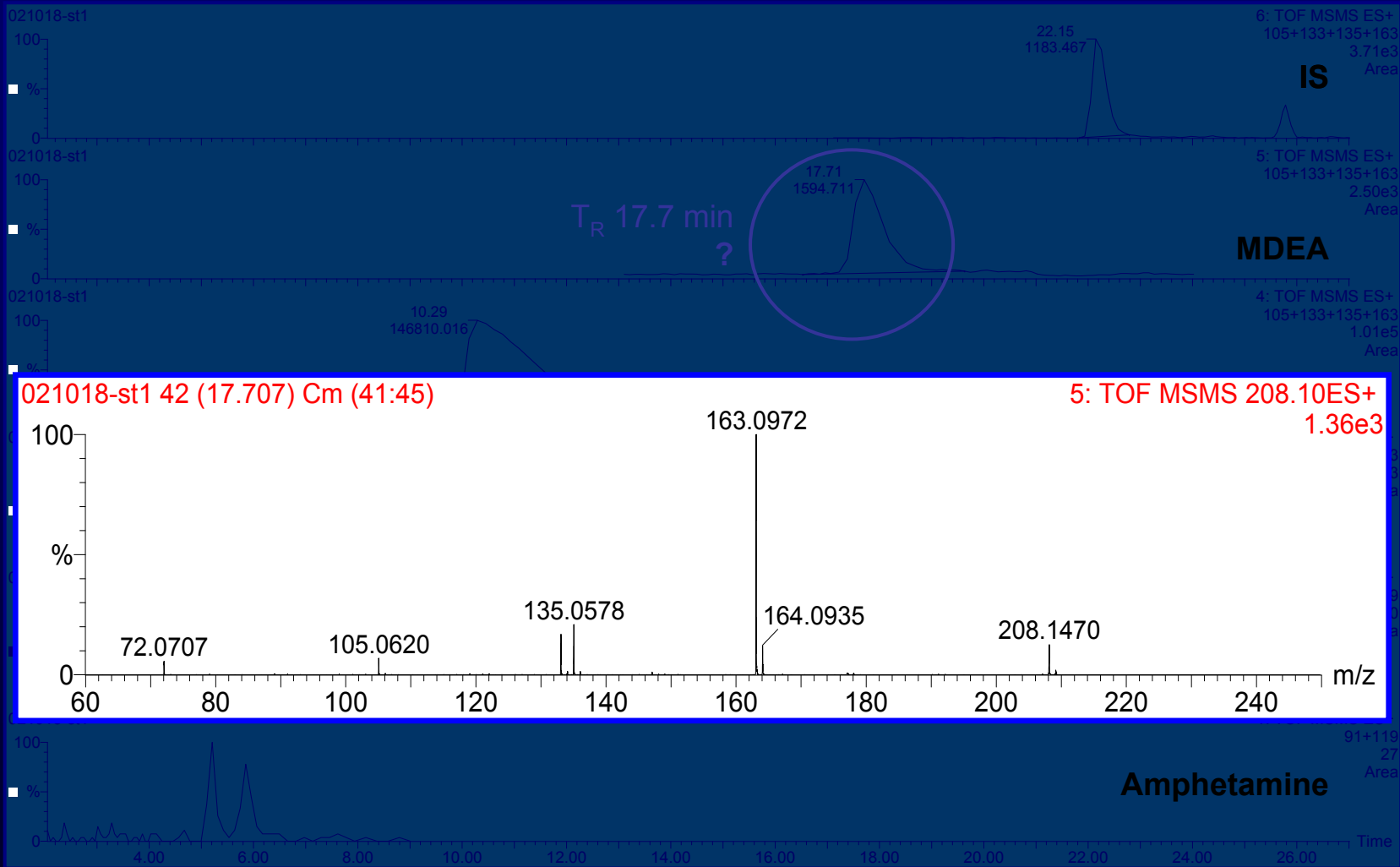
XIC calibrator 50 ng/mL MDA, MDMA, MDEA





XIC real sample (left pleural fluid extract)





XIC real sample (left pleural fluid extract)



Aim

1. Identify and quantify new substance
2. Study post-mortem distribution

→ Analytical / Chemical challenge

→ Forensic challenge



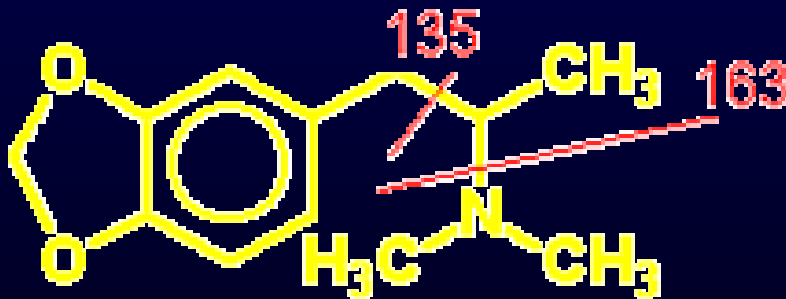
Methods

■ Identify substance (1)

- ✓ Literature overview
- ✓ Study of MSMS-spectrum: structure elucidation (MBDB, ... ?)

[MH]⁺ *m/z* 208.10

Product ions *m/z* 105; 133; 135; 163



3,4-methylenedioxy N,N-
dimethyl amphetamine

MDDM

■ Identify substance (2)

✓ In-house synthesis:

- 3,4-methylenedioxyphenylacetone
- Dimethylamine HCl
- Na-cyanoborohydride

✓ Purification:

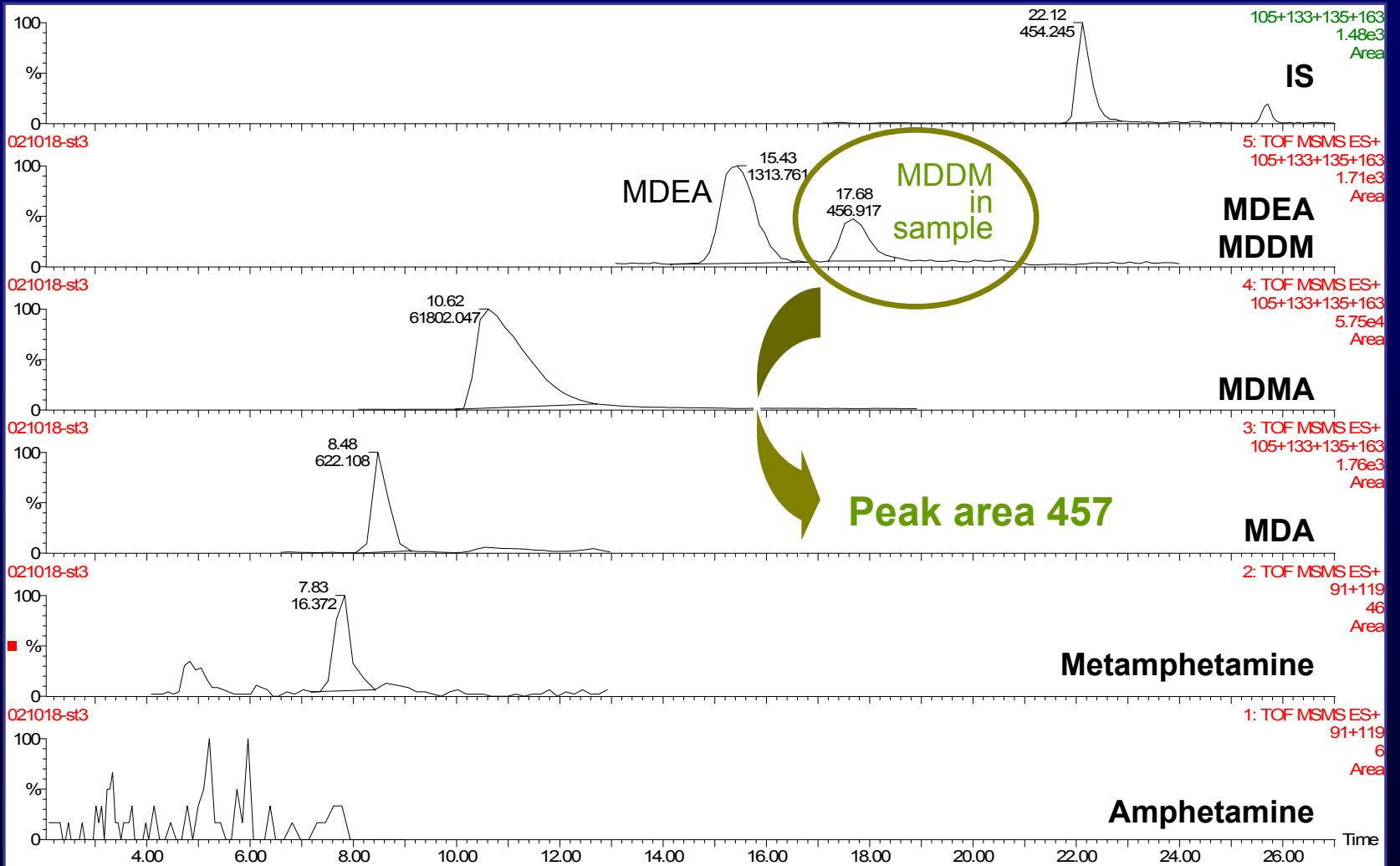
- Preparative column chromatography + fraction collection
- TLC

✓ Identity evaluation/confirmation of obtained product:

- NMR (60 MHz)
- LC-MS/MS

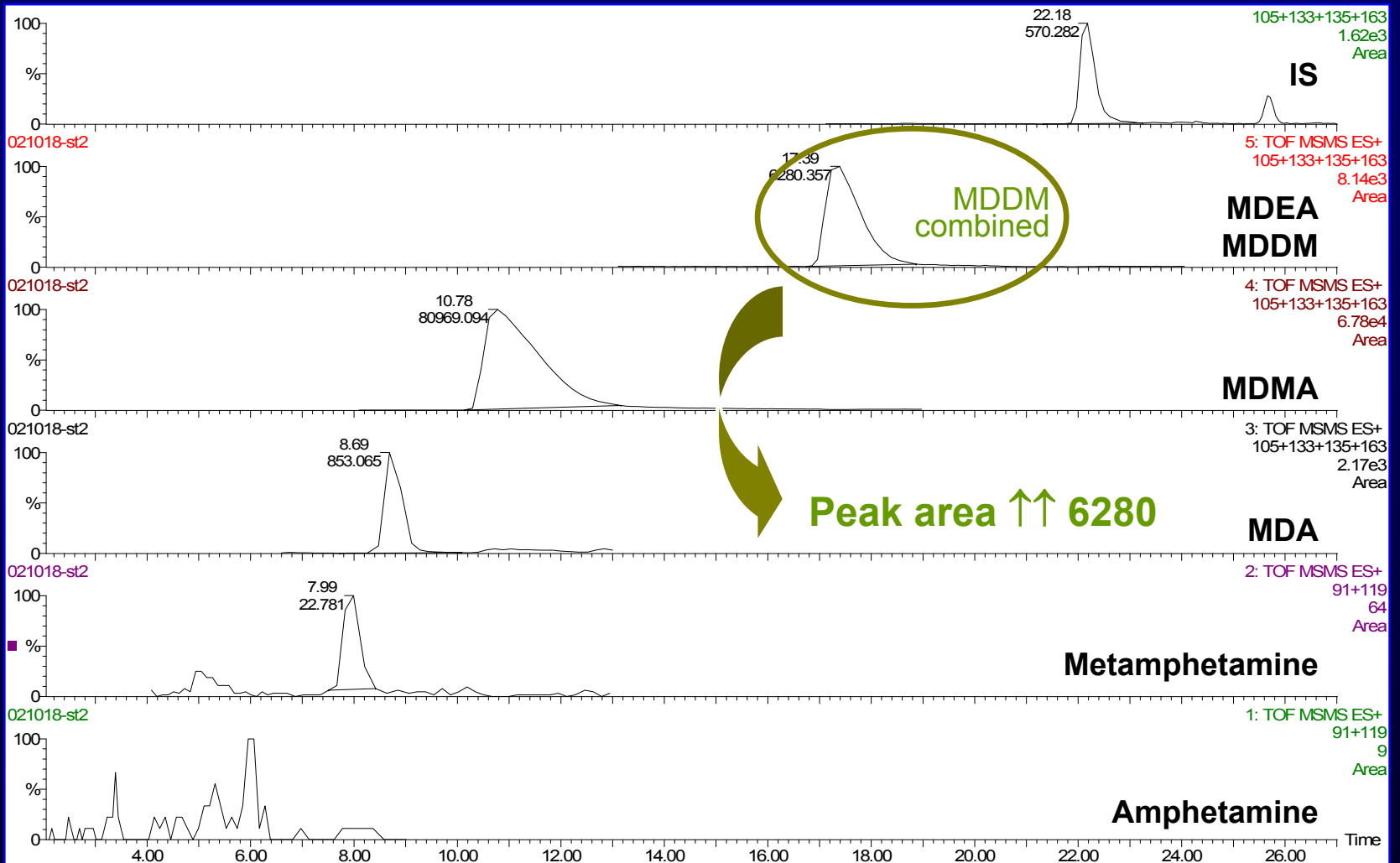
**Total yield:
450 mg MDDM**





Co-injection: real sample extract + MDEA calibrator





Co-injection: real sample extract + MDDM calibrator



■ Quantify substance

- ✓ Previously published LC-MS/MS method adapted
- ✓ Sample pretreatment:
 - L/L extraction (Hex-EtAc)
 - Back-extraction for tissues
- ✓ LC:
 - Hypersil BDS Phenyl (2.1 mm x 100 mm x 5 μ)
 - 0.2 mL/min, total runtime 32 min
 - Gradient elution: H₂O/MeOH/AcCN + 0.1 M NH₄OAc

✓ MS:

Compound	Monitored ion transition	T _R
MDA	180.10 → 105+133+135+163	8.5
MDMA	194.10 → 105+133+135+163	10.5
MDEA	208.10 → 105+133+135+163	15.5
MDDM	208.10 → 105+133+135+163	17.5
MDMPA (IS)	236.10 → 105+133+135+163	22.1

- ✓ Calibration curves: in fluid (blood, urine): 2 - 400 ng/mL
in tissue (e.g. bile, liver): 10 - 1500 ng/mL



Results

■ Specimen analysis

- Availability of specimens
- In view of post-mortem distribution evaluation

Specimen	MDDM concentration (ng/mL or ng/g)	MDMA concentration (µg/mL or µg/g)
Aortic blood	21.7	157.0
V. iliaca blood	< LLOQ	
Subclavian blood	8.2	
R pleural fluid	21.7	71.3
L pleural fluid	47.0	137.5
Femoral blood	2.5	13.5
R atrial blood	11.6	
Pericardial fluid	31.9	
Urine	42.4	71.6
Stomach contents	1113	
Bile	1101	86.9
Liver	20.3	103.5
L kidney	30.8	68.5
R kidney	39.8	155.3
R lung	12.8 - 22.6	79 -128
L lung	14.7 - 17.4	85 - 96
L cardiac muscle	13.1	214.7
R cardiac muscle	< LLOQ	65.5
Iliopsoas	< LLOQ	



Results

■ Distribution

- Femoral blood sampling = golden standard
- Post-mortem distribution from the lungs and stomach contents

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- Urinary excretion

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Conclusion

- ✓ **First report** of MDDM presence
- ✓ **Post-mortem distribution** ~ other amphetamine derivatives
- ✓ [MDDM] in ng/mL range
[MDMA] in $\mu\text{g/mL}$ range

Hypothesis: MDDM = synthesis by-product in MDMA tablets

Small amount: no influence on mechanism of death

