Estimation of mouth level smoke exposure in cigarettes with different tar content using filter analysis

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Outline

1. Background/Purpose

2. Experiment (i, ii)

   Materials and Methods
   Results

3. Summary and Conclusion

1. Background/Purpose

- ✓ **Relationships between ISO tar and nicotine yields and estimated tar and nicotine mouth level exposures (MLEs) have been reported [1, 2].**
  → **For other constituents and under other smoking conditions, the relationships between the machine-derived smoking yields and the MLEs are still not clear.**

- ✓ **A filter analysis method has been developed to estimate the MLE to cigarette smoke constituents. MLEs to four constituents (nicotine, NNK, pyrene, acrolein) have been estimated using the filter nicotine content [3].**
  → **It is not clear whether MLEs to other constituents can be estimated using filter analysis.**

Purpose:

To investigate the relationship between "machine yield" and "estimated MLE" for many constituents

1) Mariner et al. (2011) Regul Toxicol Pharmacol. 61: S39-50.
2) Nelson et al. (2011) Regul Toxicol Pharmacol. 61: S25-38.
3) Shepperd et al. (2009) Regul Toxicol Pharmacol. 55: 97-109.

Experiment (i)

Validation of a method for estimating MLE using filter nicotine content

Experiment (ii)

Estimation of MLE to each constituent in low tar cigarette (LTC) and ultra-low tar cigarette (ULTC) smokers

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2. Validation of a method for estimating MLE

Target constituents

TNCO

- Tar
- Nicotine
- Carbon monoxide

TSNAs

- NNN
- NAT
- NAB
- NNK

PAHs

- 1-Aminonaphthalene
- 2-Aminonaphthalene
- 3-Aminonaphthalene
- 4-Aminonaphthalene
- Benzo(a)pyrene

Carbonyls

- Formaldehyde
- Acetaldehyde
- Acetone
- Acrolein
- Propionaldehyde
- Crotonaldehyde
- Methyl ethyl ketone
- n-Butyraldehyde

Phenolics

- Hydroquinone
- Resorcinol
- Catechol
- Phenol
- m/p-Cresol
- o-Cresol

Organic Compounds

- 1,3-Butadiene
- Isoprene
- Acrylonitrile
- Benzene
- Toluene
- Styrene

NOx

- Nitric Oxide (NO)
- NOx

Others

- Ammonia
- Hydrogen cyanide

Target Constituents : 36

2. Validation of a method for estimating MLE

Test cigarettes

	Smoking condition	Tar (mg/cig)	Nicotine (mg/cig)	CO (mg/cig)
LTC *Low Tar Cigarette*	ISO	6	0.5	7
	HCI	23	1.6	27
ULTC *Ultra Low Tar Cigarette*	ISO	1	0.1	1
	HCI	14	1.0	20

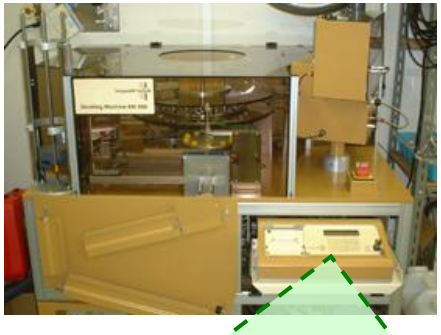
Machine yields of 36 constituents :
“ULTC < LTC” under both ISO and HCI

Smoke constituent	Each constituent (unit*)			
	ISO		HCI	
	LTC	ULTC	LTC	ULTC
Tar	5.9	0.9	23.3	13.9
Nicotine	0.51	0.09	1.64	1
Carbon monoxide	7.2	1.2	26.8	20.3
NNN	32.8	10	96.4	70.2
NAT	38.7	8.87	108	85.7
NAB	4.69	1.23	13.4	9.54
NNK	19.7	3.91	61.7	47.1
1-Aminonaphthalene	8.24	2.24	19.2	12.7
2-Aminonaphthalene	5.16	1.34	12.4	8.6
3-Aminonaphthalene	1.28	0.32	3.72	2.44
4-Aminonaphthalene	1.05	0.27	2.93	1.98
Benzo(a)pyrene	5.32	1.32	14.5	9.21
1,3-Butadiene	21.9	4.32	94.4	80.5
Isoprene	142	25.3	658	642
Acrylonitrile	3.22	0	20.8	19.5
Benzene	16.4	3.33	71	62.1
Toluene	19.1	2.81	103	86.8
Styrene	1.83	0.13	14.9	12.7
Formaldehyde	17.4	1.73	95.2	81.3
Acetaldehyde	355	64.4	1438	122
Acetone	120	23.4	516	41
Acrolein	28.9	4.35	144	136
Propionaldehyde	22.3	4.05	96.9	83.9
Crotonaldehyde	5.45	0	38.6	36.6
Methyl ethyl ketone	27.3	5.63	121	98.7
n-Butyraldehyde	14.7	4.14	55	49.9
Hydroquinone	36	7.48	96	57.4
Resorcinol	0.74	0.15	2.17	1.51
Catechol	33.4	7.25	83.9	47.8
Phenol	6.23	0.43	13.1	7.23
m/p-Cresol	5.32	0.56	11.8	6.25
o-Cresol	1.98	0.18	4.47	2.13
Nitric oxide (NO)	93.9	21.4	279	223
NOx	96.6	21.4	291	234
Ammonia	4.68	0.79	18.2	11.9
Hydrogen cyanide	48.4	2.36	356	334

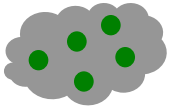
2. Validation of a method for estimating MLE

Derivation of estimation formula

Machine smoking



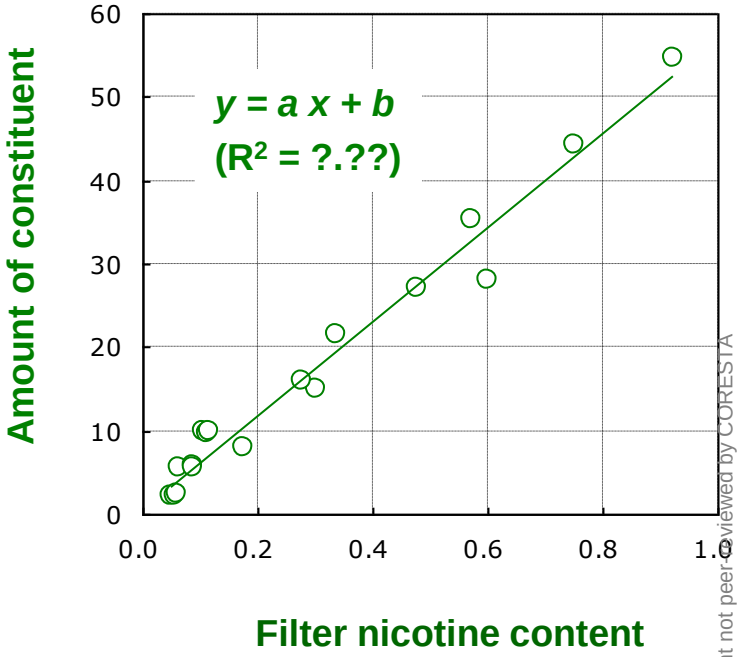
Measurement



Smoke constituent

Filter nicotine

Estimation formula (calibration curve)



18 smoking conditions

Parameter	Smoking conditions
Puff volume (ml/puff)	3 conditions 30 ml, 70 ml, 120 ml
Puff duration (sec/puff)	1 condition 2.0 sec
Inter-puff interval (sec)	3 conditions 10 sec, 30 sec, 60 sec
Butt length / Puffs (mm)/(Puffs)	2 conditions Tipping+3 mm, 3 puffs

2. Validation of a method for estimating MLE

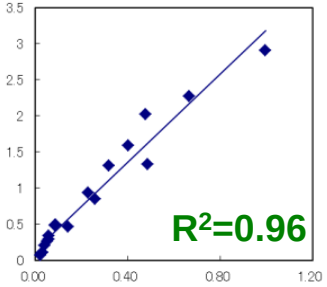
Correlation between filter nicotine content and each of the 36 constituents

Coefficient of determination R^2 derived from the calibration curves

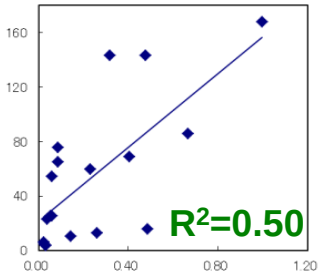
Group	Smoke constituent	LTC	ULTC
TNCO	Tar	0.97	0.99
	Nicotine	0.96	0.99
	Carbon monoxide	0.91	0.95
Tobacco Specific Nitrosamines	NNN	0.96	0.98
	NAT	0.94	0.99
	NAB	0.92	0.99
	NNK	0.95	0.99
Polycyclic Aromatic Hydrocarbons	1-Aminonaphthalene	0.92	0.95
	2-Aminonaphthalene	0.89	0.90
	3-Aminonaphthalene	0.93	0.97
	4-Aminonaphthalene	0.93	0.97
	Benzo(a)pyrene	0.97	0.98
Organic Compounds	1,3-Butadiene	0.85	0.88
	Isoprene	0.89	0.93
	Acrylonitrile	0.84	0.89
	Benzene	0.89	0.93
	Toluene	0.90	0.94
	Styrene	0.83	0.84

Group	Smoke constituent	LTC	ULTC
Carbonyls	Formaldehyde	0.50	0.43
	Acetaldehyde	0.88	0.94
	Acetone	0.90	0.95
	Acrolein	0.83	0.84
	Propionaldehyde	0.88	0.93
	Crotonaldehyde	0.82	0.87
	Methyl ethyl ketone	0.88	0.94
	n-Butyraldehyde	0.88	0.95
Phenolics	Hydroquinone	0.93	0.98
	Resorcinol	0.93	0.95
	Catechol	0.90	0.99
	Phenol	0.78	0.88
	m/p-Cresol	0.83	0.92
	o-Cresol	0.87	0.93
Nitrogen Oxides	Nitric oxide (NO)	0.91	0.94
	NOx	0.91	0.95
Others	Ammonia	0.89	0.92
	Hydrogen cyanide	0.85	0.90

Nicotine (LTC)



Formaldehyde (LTC)



Except for formaldehyde, a strong correlation was found between the filter nicotine content and each of the 35 constituents in both types of cigarette (R^2 = 0.78 – 0.99).

MLEs to 35 constituents can be estimated using the filter nicotine content.

Experiment (i)

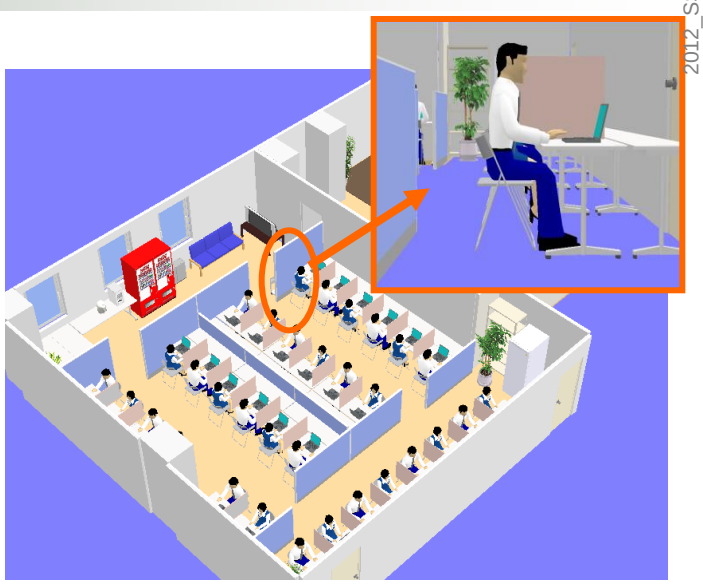
Validation of a method for estimating MLE using filter nicotine content

Experiment (ii)

Estimation of MLE to each constituent in low tar cigarette (LTC) and ultra-low tar cigarette (ULTC) smokers

2. Estimation of MLE in smokers

Study design



- ✓ **Subject number:**
  210 smokers
  (LTC smokers: 105, ULTC smokers: 105)

- ✓ **Inclusion criteria:**
  - Japanese male smokers
  - Aged 21-49 years
  - Smoking the same brand for at least 3 months, 10 or more cigarettes per day

- ✓ **Smoking Condition:**
  Smoke their own brand of cigarettes ad libitum for 7 hours (10:30-17:30)

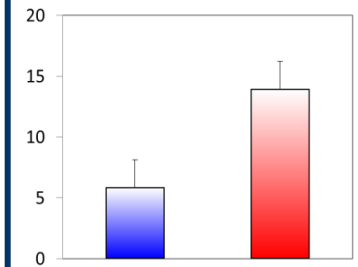
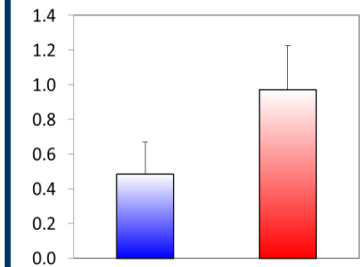
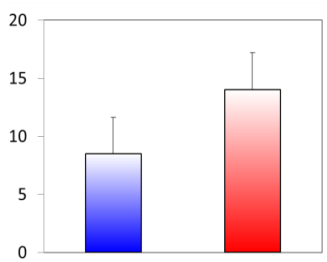
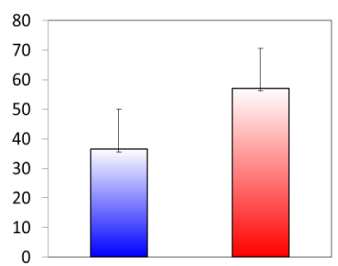
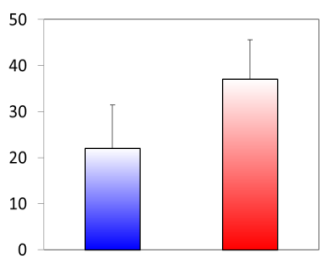
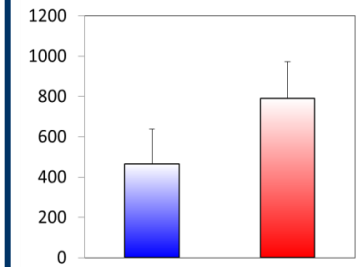
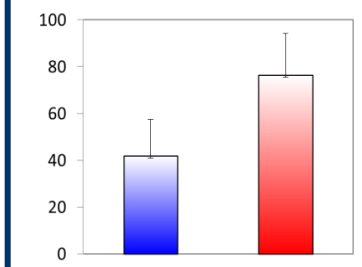
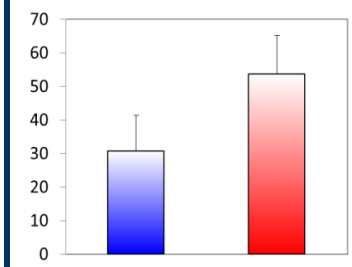
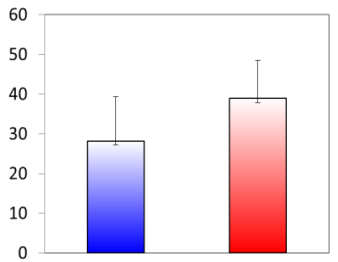
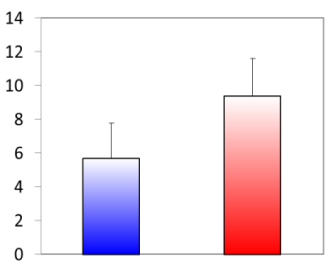
- ✓ **Items investigated:**
  - Filter nicotine content
  - Estimation of MLE to 35 validated constituents using the filter nicotine content

2. Estimation of MLE in smokers

Estimated MLE in smokers

X-axis: ULTC LTC

Y-axis: Estimated MLE

Tar (mg/cig)	Nicotine (mg/cig)	CO (mg/cig)	NNN (ng/cig)	NNK (ng/cig)
				
Acetaldehyde (µg/cig)	**Acrolein (µg/cig)**	**1,3-Butadiene (µg/cig)**	**Benzene (µg/cig)**	**Benzo(a)pyrene (ng/cig)**
				

Mean ±SD

Estimated MLEs to all 35 constituents in ULTC smokers are statistically significantly lower than those in LTC smokers

3. Summary and Conclusion

Summary

- ✓ **Validation of a method for estimating MLE**

  Except for formaldehyde, MLEs to 35 constituents can be estimated using the filter nicotine content.

- ✓ **Estimation of MLE to each constituent in smokers**

  Estimated MLEs to 35 constituents in ULTC smokers are lower than those of LTC smokers.

Conclusion

- ✓ **The relationship between “machine yield” and “estimated MLE”**

  Machine yield of 35 constituents
  under both ISO and HCI; ULTC < LTC
  Estimated MLE to 35 constituents ; ULTC < LTC

  → **Machine yield and estimated MLE were correlated for both LTC and ULTC in this study.**

Additional investigation

Application of ratio values

✓ **Recently, some researchers have reported the "ratio value" as an index obtained by machine smoking.**

1) Each constituent/nicotine [1].

For machine yields in US cigarettes, the ratio value provided an inverse ranking of tar categories in many cases.

Each constituent : "Ultra-Lights"<"Lights"<"Full Flavor"

Each constituent/nicotine : "Ultra-Lights">"Lights">"Full Flavor"

2) Tar/nicotine (T:N ratio) [2]

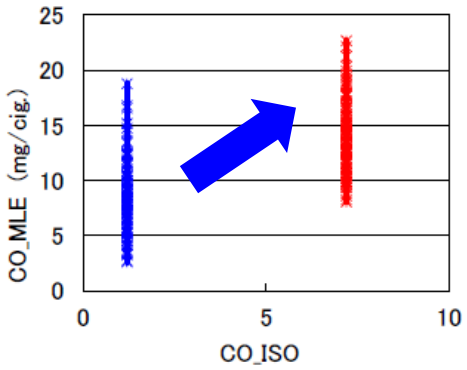
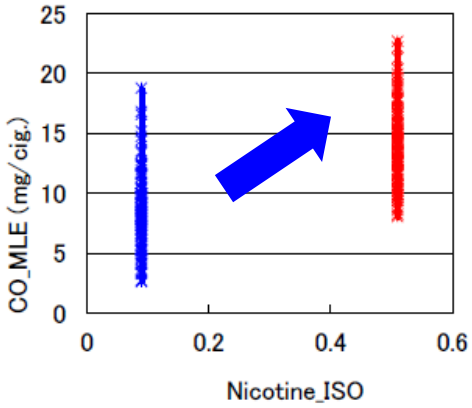
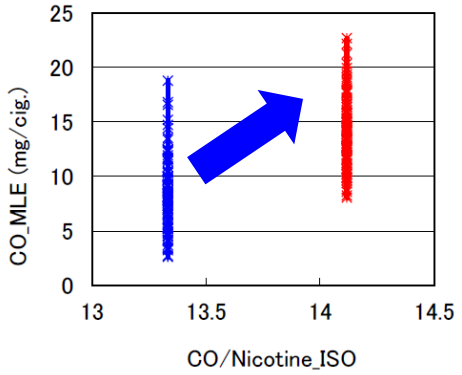
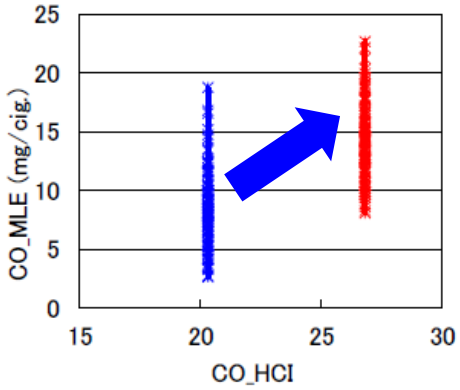
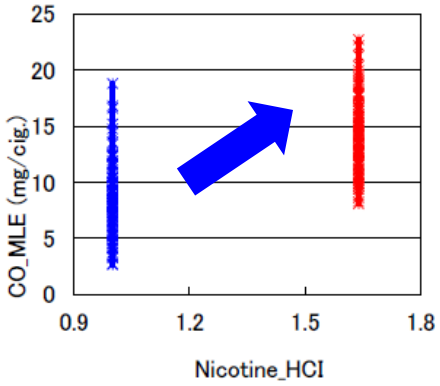
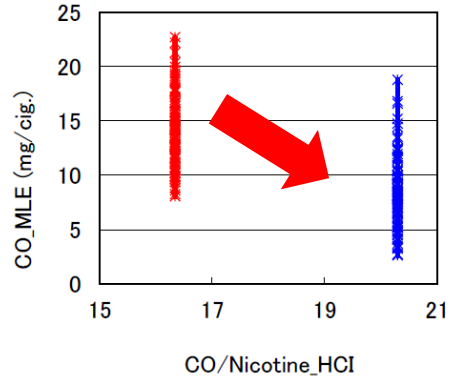
The ratio value was affected by the smoking conditions.

Investigation of the relationship between "estimated MLE" and "ratio values; each constituent/nicotine and each constituent/tar" under ISO and HCI conditions.

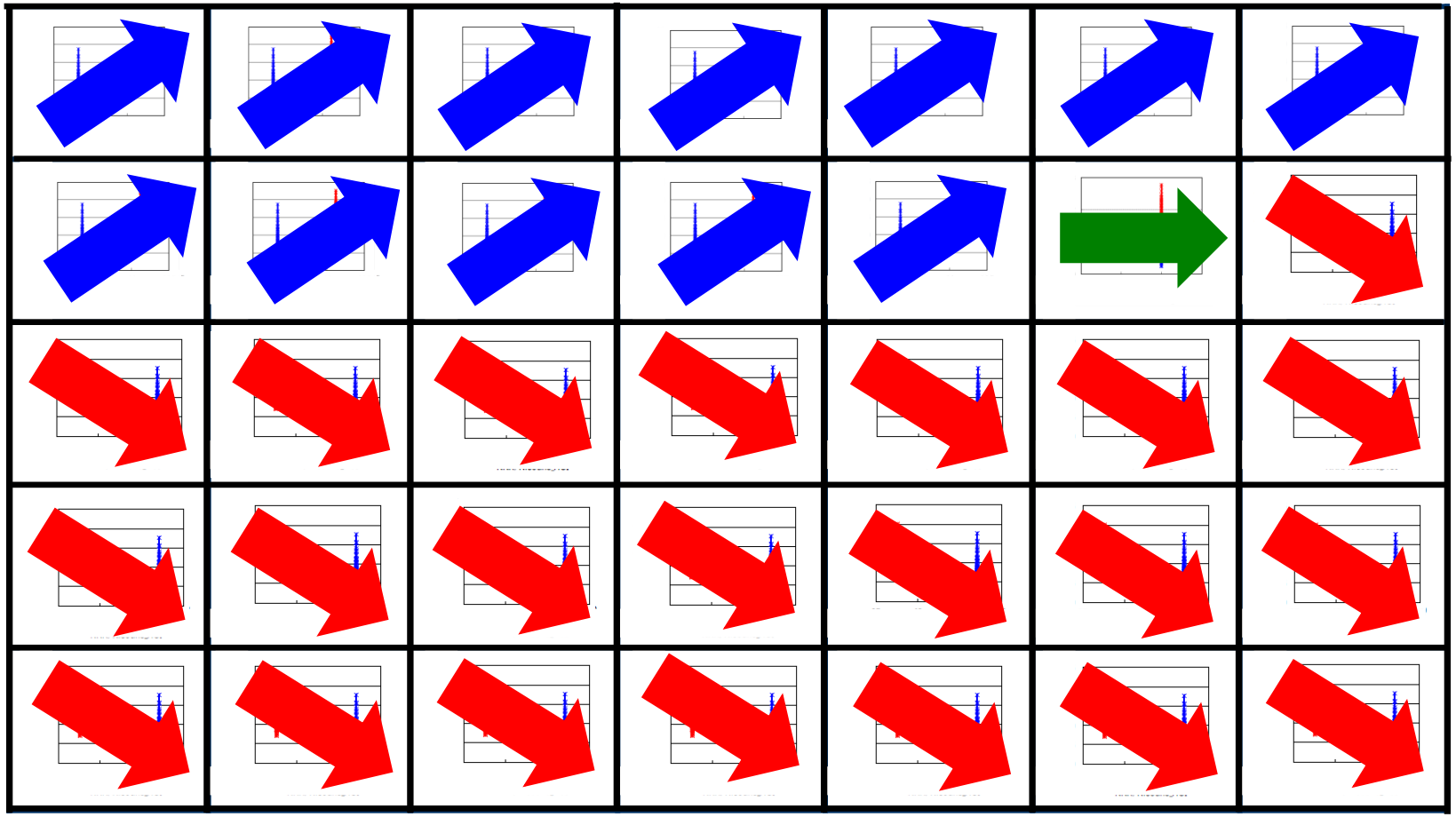
1)Bodnar et al. (2012) Regul Toxicol Pharmacol. 64: 35-42.
2)Nelson et al. (2011) Regul Toxicol Pharmacol. 61: S25-38

Application of CO/nicotine under ISO and HCI

* : LTC smokers * : ULTC smokers

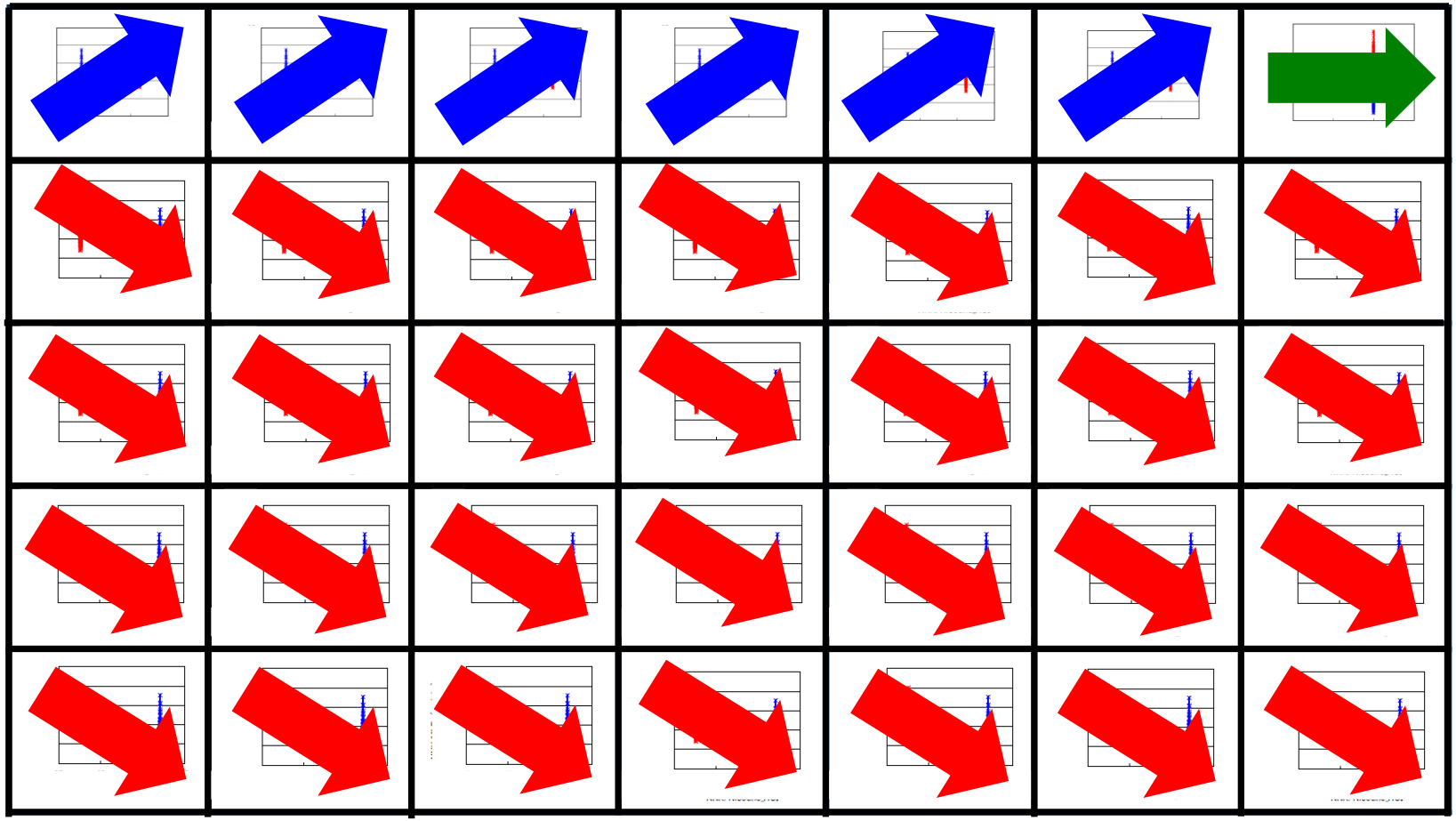
	CO	Nicotine	CO/nicotine
ISO			
HCI			

Relationship between estimated MLE and each constituent/nicotine under ISO



Each constituent/nicotine under the ISO had an inverse relationship to estimated MLE in 22 of 35 constituents.

Relationship between estimated MLE and each constituent/nicotine under HCI



Each constituent/nicotine under the HCI had an inverse relationship to estimated MLE in 28 of 35 constituents.

Overview

Number of constituents which showed inverse relationship

Smoking condition	Ratio values obtained by machine smoking	
	Each constituent / nicotine	Each constituent / tar
ISO	22	25
HCI	28	30

In many cases, the order of ratio values (ULCT>LTC) have an inverse relationship to estimated MLE (ULCT<LTC).

In this study, only two cigarettes were used, LTC and ULTC.
It is necessary to conduct further studies using other cigarettes in order to clarify the relationship between the estimated MLE and ratio values obtained by machine smoking.

Thank you for your attention !