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COMPARISON OF OPERATIONAL JET FUEL AND NOISE EXPOSURES: FUEL EXPOSURE RESULTS

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14. ABSTRACT
The study purpose was to examine effects on hearing in flight line personnel with combined exposure to jet fuel and noise. We analyzed fifteen volatile organic compounds (VOCs) jet fuel components in personal air samples, blood and urine at Japan Air Self Defense Force (JASDF) and United States Air Force (USAF) air bases. There were 168 subjects who voluntarily joined this study at 5 JASDF air bases (ABs) and 2 USAF ABs in Japan. Subjects were divided into eight groups: CJ, Non-exposed control subjects in JASDF; CK, Non-exposed control subjects at Kadena; CM, Non-exposed control subjects at Misawa; T-4, JetA1 exposed T-4 flight line crews at Matsushima and Hamamatsu; F-2, JetA1 exposed F-2 flight line crews at Matsushima; F-4, JP-4 exposed F-4 flight line crews at Hyakuri; F-15, JP-8 exposed F-15 flight line crews at Kadena; F-16, JP-8 exposed F-16 flight line crews at Misawa. Only total VOCs of all samples of F-4 were higher than those of the control group for the same AB. Benzene was found at high frequencies and concentrations in all samples for the F-4. These results are characteristic of JP-4 exposure, which due to higher volatility, has a different composition than JP-8 and JetA1.

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1.0 SUMMARY

Hearing loss is still prevalent in various occupational environments. Flight line personnel are constantly exposed to noise while working in and around aircraft. They are also exposed to exhaust from the jet fuel. Recent studies suggested jet fuel in combination with noise are more associated with hearing loss than with noise exposure alone. Therefore, flight line personnel may be more likely to develop hearing loss. The purpose of this study was to examine the effects on hearing in flight line personnel with combined exposure to jet fuel and noise and to identify and address gaps in data for flight line personnel. This study was a collaborative research effort between the Japan Air Self-Defense Force (JASDF) and the US Air Force (USAF). The JASDF analyzed jet fuel components as fifteen volatile organic compounds (VOCs) in personal air samples for the flight line air environment, blood and urine at air bases (ABs) in Japan. The USAF analyzed noise dosimetry, miRNA biomarkers, metabonomic biomarkers and an audiometric test battery, consisting of immittance measurements, audiogram, otoacoustic emissions (OAE) and auditory brain response (ABR). This report describes the characteristics of VOCs exposures for the flight line environment (air, blood and urine) in each aircraft and fuel type. The analytical methods and results of noise dosimetry, miRNA biomarkers, metabonomic biomarkers and an audiometric test battery are described in the USAF final report.

One hundred and sixty-eight subjects voluntarily joined this study in both JASDF ABs (Hamamatsu, Matsushima, Hyakuri, Yokota and Iruma) and USAF ABs (Kadena and Misawa) in Japan. The subjects were divided into eight groups: CJ, Non-exposed control subjects in JASDF; CK, Non-exposed control subjects in Kadena; CM, Non-exposed control subjects in Misawa; T-4, JetA1 exposed T-4 flight line crews in Matsushima and Hamamatsu; F-2, JetA1 exposed F-2 flight line crews in Matsushima; F-4, JP-4 exposed F-4 flight line crews in Hyakuri; F-15, JP-8 exposed F-15 flight line crews in Kadena; F-16, JP-8 exposed F-16 flight line crews in Misawa.

Samples (personal air, blood and urine) were collected according to the typical sequence of events at each base. To measure the personal air samples during shift, prior to shift each subject had a personal air monitor put in place. Blood draws were conducted post shift. Urine samples (entire void) were collected prior to shift (early morning first void) and post shift. We measured 15 VOCs to include 10 straight chain alkanes (n-Hexane, n-Heptane, n-Octane, n-Nonane, n-Decane, n-Undecane, n-Dodecane, n-Tridecane, n-Tetradecane and n-Pentadecane) and 5 aromatic hydrocarbons (Benzene, Toluene, Ethylbenzene, m,p-Xylene and o-Xylene) in personal air samples, blood and urine.

Total VOCs in personal air samples in each group were extremely low compared to the permissible limits recommended by the Japan Society for Occupational Health (JSOH) and the Occupational Safety and Health Administration (OSHA). Such trace amounts of VOCs are also known to occur in carpet and wallpaper adhesives and can be detected in

office and home environments. Only total VOCs of all samples (air sample, blood and urine prior to and post shift) of the F-4 group were higher than those of the control group at the same AB. Benzene was found at high frequencies and concentrations in the personal air samples, blood, and urine prior to and post shift in F-4. This may be due to differences in the composition of the respective jet fuels (JP-4 vs. Jet A1/JP-8) and the performance of the respective jet engines.

Total VOCs in the personal air samples of each group were very low compared to the acceptable limits recommended by the JSOH and OSHA and were not considered to cause adverse health effects in the flight line personnel. Only total VOCs of all samples (air, blood and urine prior to and post shift) of F-4 were higher than those of the control group for the same AB. Benzene was found at high frequencies and concentrations in the personal air samples, blood, and urine prior to and post shift for the F-4 group. These results may be characteristic of JP-4 exposure, which has a different composition than JP-8 and JetA1.

2.0 INTRODUCTION

2.1 Purpose

Hearing loss is prevalent in various occupational environments. People who work in and around aircraft are at risk of developing hearing loss. Studies have shown that pilots, flight crews, aircraft technicians and mechanics have high rates of hearing loss compared to unexposed populations from analyses of large epidemiological databases (Fitzpatrick, 1988; Jaruchinda et al., 2005). Aircraft technicians and mechanics in the commercial aviation industry were found to have higher hearing thresholds at younger ages (30 to 40 years) compared to age-matched reference groups (Smedje et al., 2011). In addition, military fighter and helicopter pilots are known to be at high risk of developing hearing loss compared to commercial pilots (Raynal et al., 2006). Hearing loss typically takes on a high frequency sloping configuration, even with the use of hearing protection such as earplugs, headsets or helmets (Jaruchinda et al., 2005).

A retrospective cohort study was conducted by Williams et al. (2015) using data from the U.S. Department of Defense occupational and environmental health database to compare JP-8 exposed individuals with hearing test results. Hearing tests were compared for personnel exposed to noise and those exposed to both noise and JP-8 from 1996 to 2013. Personnel aged 17-44 years who were exposed to JP-8 were more likely to have an occupational hearing shift than their non-exposed peers of the same age. When the mean threshold change was examined between the first and last audiogram of the personnel, a statistically significant difference was found at 3,000 Hz and 4,000 Hz in the JP-8-exposed group. The results of this epidemiological study suggest a synergistic effect on hearing loss when workers are exposed to both noise and JP-8.

The US Armed Services and the North Atlantic Treaty Organization (NATO) have adopted JP-8 as their standard fuel (Fechter et al., 2012; Merchant-Borna et al., 2012). The Japan Air Self-Defense Force (JASDF) switched to Jet A1, which is JP-8 without additives. The US Air Force (USAF) now designates Jet A with the current AF performance additives as F-24. Jet A and Jet A1 are very similar in chemical composition. The main physical difference between the two is the freezing point of the fuel. Jet A is mainly used in the U.S. commercial aviation industry.

Preliminary epidemiological analyses of auditory records from aircraft maintenance personnel exposed to both noise and jet fuel (primarily the more volatile JP-4) suggest that concurrent exposure may potentiate hearing loss at jet fuel concentrations below the currently-established safe occupational exposure limit (Kaufman et al., 2005). Potentiation of hearing loss was confirmed in experiments where rats were exposed to JP-8 and non-damaging noise levels (Fechter, Gearhart and Fulton, 2010). Recent animal studies have revealed that exposure to JP-8 combined with noise may result in the loss of pre-neural cochlear sensitivity as shown by suppression of distortion product otoacoustic emissions (DPOAE), increased auditory thresholds and depletion of cochlear sensory cells as evidenced by cytocochleograms that plot the percentage of missing outer hair cells (Fechter et al., 2007, 2010, 2012). In the experimental animal models, the effect of combining jet fuel plus noise exposures was greater than that of the individual exposures to jet fuel or noise. An additional study by Guthrie et al. (2014) examined the same functional and structural assays of the presynaptic sensory cells, but added neurophysiologic studies of the auditory pathway, by conducting the ABR test. Results revealed that peripheral auditory function was not affected by individual exposures and there was no effect when the exposures were combined using this exposure paradigm and animal model. However, brainstem encoding of stimulus intensity measured by auditory brainstem response was impaired. All of these findings are particularly important because military and government regulations regarding toxic exposures are often based on exposure to a single agent and less is known about combined exposure to jet fuel and noise.

A review of recent literature by (Warner, Fuente and Hickson, 2015) examined the effects of combined exposure to JP-8 jet fuel (or its aromatic solvent components) and noise on the auditory nervous system in humans. Their search found 178 articles but only 37 were relevant enough to be examined further. After articles with animal models, or about a solvent not in jet fuel or an article in a conference proceedings without sufficient data were removed, a total of six articles met the inclusion criteria and were summarized in their review. One article was by Kaufman et al. (2005) cited above where exposure was to JP-4 jet fuel only. The other five (three by the second author A. Fuente) examined the effects of individual solvents or mixed solvents. The conclusions of the literature review suggest that there is an association between aromatic solvents and jet fuel, in combination with noise and central auditory dysfunction/hearing loss. The articles considered in this review indicate that the assessment of the auditory nervous system, including pure-tone audiometry; DPOAE; auditory brainstem response, and behavioral functional assessments, should be conducted as part of a comprehensive test battery for military members exposed to both noise and solvents in the workplace. This study plus the literature in general supports the need for a closer investigational paradigm created to survey and document the auditory and environmental exposures for relating hearing decrement assessment for flight line personnel.

A previous collaborative research effort between the JASDF and the USAF correlated exposure and biomarkers for JP-4 and compared them with those from JP-8 (Kobayashi et al., 2014; Mattie et al., 2014). The JASDF measured jet fuel components in air, blood and urine, while the USAF analyzed for biomarkers. Personal exposure of 48 volatile organic compounds (VOCs) was measured in F-15 and C-130 flight line crews, and non-exposed control subjects (mainly hospital workers). This study suggested that the level of exposure to jet fuel is dependent on the type of aircraft and fuel. Moreover, the disposition of VOCs is that workers in operational environments are exposed through the lungs with entry into the blood, are metabolized resulting in metabolites in the urine. A direct human exposure response comparison study during military operations, able to evaluate by characterizing jet fuel components and their amounts in blood, urine and within flight line air environment, was necessary to draw substantive conclusions regarding the combined jet fuel and noise exposures and specific auditory health effects of flight line personnel.

The purpose of this study was to examine the effects on hearing in flight line personnel with combined exposure to jet fuel and noise and to identify and address gaps in data for flight line personnel. This report showed the characteristics of VOCs exposures in flight line environment in each aircraft and fuel type.

2.2 Collaborative research

This study was a collaborative research effort between the JASDF and the USAF. The JASDF analyzed jet fuel components as fifteen VOCs in personal air samples from the flight line air environment, blood and urine at air bases (ABs) in Japan, while the USAF analyzed noise dosimetry, miRNA biomarkers, metabonomic biomarkers and an audiometric test battery, consisting of immittance measurements, audiogram, otoacoustic emissions (OAE) and ABR. The analytical methods and results of noise dosimetry, miRNA biomarkers, metabonomic biomarkers and an audiometric test battery are described in the USAF final report.

3.0 METHODS AND SUBJECTS/DEMOGRAPHIC DATA

3.1 Subjects

3.1.1 Recruitment

The study was designed to recruit the following total number of flight line personnel subjects: 30 to 50 individuals from F-15 or F-16 USAF ABs exposed to JP-8; 30 to 50 individuals from one or more T-4, F-2 or F-4 ABs exposed to JP-4 or Jet A1. Non-exposed control subjects needed to be mainly medical personnel sampled in an identical manner as flight line personnel: matched to the number of flight line personnel number (30 to 50) for JP-8 at U.S. ABs and matched to number of flight line personnel number (30 to 50) for JP-4/Jet A1 from JASDF ABs. Non-exposed control subjects in JASDF were recruited from Yokota and Iruma ABs because there are only a few medical personnel who are non-exposed control subjects in Hamamatsu, Matsushima and Hyakuri ABs.

Subjects were volunteers who were active duty (JASDF and USAF) flight line personnel. Subjects could be male or female and the age had to be under 35 years old. Subjects were questioned about audiological history and the following demographic information: Name (was in header, was cut off after sampling was completed and replaced with a base specific number); Career field; Rank; Years of service; Age; Gender; Hobbies (other fuel or solvent exposures; worked on car or truck engines, either on or off duty); and Last time they fueled a government or personal vehicle and type of fuel.

3.1.2 Demographic data

There were 168 subjects who voluntarily joined this study in 5 JASDF ABs and 2 USAF ABs in Japan (Table 1).

Table 1. Number of subjects and sampling date at each air base

Date	Air Base	Aircrafts	Jet fuel	Assignment	Number of Subjects
30 May - 8 June 2018	Hyakuri JASDF	F-4	JP-4	The 301st SQ The 302nd SQ	20
		Control		7th Air Wing Air Base Group (Medical workers)	2
11 June - 12 June 2018	Yokota JASDF	Control		Operations Support Wing (Medical workers)	5
13 June - 15 June 2018	Iruma JASDF	Control		Aeromedical Laboratory (Medical workers)	11
19 March - 10 April 2019	Kadena USAF	F-15	JP-8	The44th SQ The 67th SQ	23
		Control		The 18th Med Gr (Medical workers)	22
8 November - 12 November 2021	Matsushima JASDF	T-4	JetA1	The 21st SQ	7
		F-2		The 11th SQ	7
6 December - 10 December 2021	Hamamatsu JASDF	T-4	JetA1	The 31st SQ The 32nd SQ	22
11 July - 22 July 2022	Misawa USAF	F-16	JP-8	The14th SQ	18
		Control		The 35th Med Gr (Medical workers)	15
21 October – 27 October 2022	Iruma JASDF	Control		Aeromedical Laboratory (Medical workers)	16
Total number					168

The subjects were divided into eight groups: CJ, Non-exposed control subjects in JASDF; CK, Non-exposed control subjects in Kadena; CM, Non-exposed control subjects in Misawa; T-4, JetA1 exposed T-4 flight line crews in Matsushima and Hamamatsu; F-2, JetA1 exposed F-2 flight line crews in Matsushima; F-4, JP-4 exposed F-4 flight line crews in Hyakuri; F-15, JP-8 exposed F-15 flight line crews in Kadena; F-16, JP-8 exposed F-16 flight line crews in Misawa (Table 2). Mean age of the F-15 group was significantly lower than CJ, CK, CM and T-4. The mean age of the F-16 group was also significantly lower than CK and CM. No significant differences were found among the other groups. Working experience years of the F-15 group was significantly lower than the other groups except for CJ and F-16. The smoking rates were higher in the jet fuel exposed groups (T-4, F-2, F-4, and F-15: 35.0 - 71.4 percent (%)) with the exception of the F-16 group (16.7%) than in the control groups CJ, CK and CM (22.7 - 26.7%). The proportion of female subjects was higher in the control groups (20.6 - 50.0%) than in the jet fuel exposed groups (0 - 16.7%).

Table 2. Summary of demographic data

	Control			Jet fuel exposure					statistically significant difference
	CJ	CK	CM	T-4	F-2	F-4	F-15	F-16	
Number	34	22	15	29	7	20	23	18	
Fuel	N/A			JetA1		JP-4	JP-8		
Age±SEM (yrs)	27.9±1.0	29.6±1.0	31.3±1.3	26.9±0.8	26.6±1.7	25.2±1.1	22.6±0.6	23.9±0.8	CJ > F-15 CK > F-15 CM > F-15 T-4 > F-15 CK > F-16 CM > F-16
Work experience±SEM (yrs)	6.0±1.2	8.3±1.1	8.7±1.2	7.2±0.9	7.0±1.8	6.5±1.0	2.5±0.4	4.4±0.7	CK > F-15 CM > F-15 T-4 > F-15 F-2 > F-15 F-4 > F-15
Smokers (%)	9 (26.5)	4 (18.2)	4 (26.7)	13 (44.8)	5 (71.4)	7 (35.0)	9 (39.1)	5 (27.7)	
Female (%)	7 (20.6)	11 (50.0)	6 (40.0)	7 (24.1)	0	0	1 (4.3)	3 (16.7)	

Abbreviations: SEM, standard error of the mean.

3.2 Methods for Sampling and Analysis

3.2.1 Sampling of personal air, blood and urine

Samples (personal air, blood and urine) were collected according to the typical sequence of events at each base. At end of shift, questions were asked about exposures during shift as well as a brief summary of work activities associated with jet fuel and jet exhaust including time on flight line (location of job, physical activities). Additional questions were about exposure to any spills of any kind; any direct dermal exposure to jet fuel or any solvent or other exposures such as solvents and cleaning fluids; were they a smoker (if yes, number of cigarettes, cigars, heated tobacco products and/or vape smoked) and how much caffeine did they consume.

The sampling schedule for the study is shown in Table 3. To measure the personal air samples during shift, prior to shift each subject had a personal air monitor put in place. Blood draws were conducted post shift. Each subject had their blood drawn at the clinic, base hospital or an approved designated area for that base. Each subject had 15 milliliters (mL) of blood drawn into the following tubes: One 5 mL blood collection tube for chemical analysis with heparin (Venoject II®, Terumo, Tokyo, JP) and Two 2.5 mL PAXgene Blood RNA tubes for biomarkers associated with RNA in leukocytes (one 5 mL tube as alternative (see below)). Urine samples (entire void) were collected prior to shift (first void in early morning) and post shift. These samples were to determine if blood and urine levels of jet fuel components and potential biomarkers were present post shift. The pre-shift urine sample was required as a baseline for metabolomics.

Table 3. Sampling schedule

Prior to Shift	**During Shift**	**Post Shift:** after flight line operations
- collect urine	- perform work duties as usual	- remove personal air sampler and noise dosimeter
- place personal air sampler		- draw blood
- place noise dosimeter		- collect 2nd urine

3.2.2 VOCs

We measured 15 VOCs which included 10 straight chain alkanes: n-Hexane, n-Heptane, n-Octane, n-Nonane, n-Decane, n-Undecane, n-Dodecane, n-Tridecane, n-Tetradecane and n-Pentadecane and 5 aromatic hydrocarbons: Benzene, Toluene, Ethylbenzene, m,p-Xylene and o-Xylene in personal air samples, blood and urine.

3.2.3 Personal air samples

A Personal Air Monitor (PAS-500) was placed into a pocket of a vest worn by the subject (Figure 1). The monitor went into the chest pocket with just the tip of the charcoal tube (ORBO32 small, SUPELCO, Bellefonte, PA) extending from the pocket. Prior to the analysis, the charcoal was removed from the tube. VOCs as well as higher chain compounds (up to C15 and C16) were extracted from the charcoal using carbon disulfide. The sample extracts were analyzed using a gas chromatograph with a flame ionization detector (Gas Chromatography-Flame Ionization Detector (GC-FID), Shimadzu Corporation, Kyoto, Japan) for hydrocarbons, BP 36°-216 °C and aromatic hydrocarbons according to the standard NIOSH Methods: 1500, Issue 3: 15 March 2003 and 1501, Issue 3: 15 March 2003, respectively.

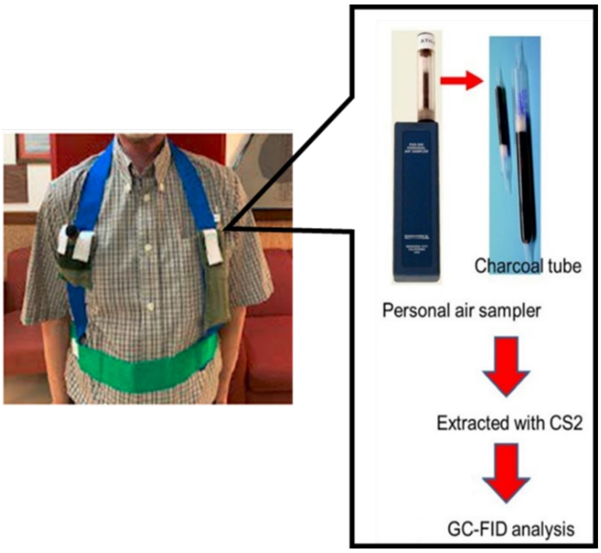


Figure 1: Personal air sampling device and analytical scheme for VOCs. The pocket on the left (right side of person) contained a noise dosimeter that will be described in the USAF report. Personal Air Monitor (PAS-500) and charcoal tube (ORBO32 small, SUPELCO). **(image is David Mattie – one of the authors)**

3.2.4 Blood

The whole blood sample for chemical analysis was stored chilled (4 degrees (°) Celsius (C)) in the dark until analysis. A 3 mL of portion of whole blood was transferred to 15 mL SPME (solid phase micro-extraction) headspace vials. Samples were spiked with 20 microliters (µL) of an internal standard mixture. Samples were analyzed by Gas Chromatography-Mass Spectrometer Detector (GC/MSD) in electron ionization (EI) mode using a Shimadzu GC/MS TQ8040-NX (Figure 2). Two 2.5 mL PAXgene Blood RNA tubes for biomarkers associated with RNA in leukocytes were frozen and stored frozen until analysis. Those frozen blood samples were shipped to the USAF/711 HPW at Wright-Patterson AFB.

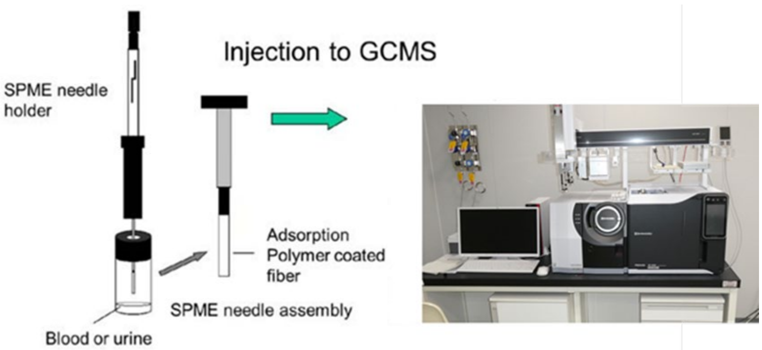


Figure 2: Schematic illustrations of SPME extraction with GCMS (Shimadzu GC/MS TQ8040-NX)

3.2.5 Urine

Urine weight was recorded and then 1mL of urine was added into one vial, 3 mL of urine each was placed into three vials, 5 mL of urine was transferred into one vial and10 mL of urine each went into three vials. The 10 mL of urine sample for chemical analysis was stored chilled (4°C) in the dark until analysis. The 1 mL, 3 mL and 5 mL of urine were frozen and stored frozen until analysis. Three 10 mL samples were for chemical analysis by AML to analyze for jet fuel components. Briefly, urine was transferred to a SPME headspace vial. The sample was spiked with an internal standard mixture. Samples were analyzed for jet fuel components by GC/MS in EI mode using a Shimadzu GC/MS TQ8040-NX and reported per 100 micrograms (μg) of creatinine (Cr). The one 1 mL, three 3 mL and one 5 mL frozen samples were shipped to the USAF/711 HPW at Wright-Patterson AFB.

3.2.6 Statistical analysis

The comparison of mean age, working experience years and concentrations of total VOCs in the personal air samples, blood and urine among each group was completed using Mann-Whitney U-tests with Bonferroni correction. A p-value < 0.0018 (0.05 / 28) was considered statistically significant difference. The comparison of total VOCs in urine prior to shift and post shift, in the smokers and the non-smokers was completed using Wilcoxon signed-rank test. A p-value < 0.008 (0.05 / 6) was considered statistically significant difference. All analyses were conducted in SPSS (version 24, SPSS Inc., Chicago, IL, USA).

4.0 RESULTS AND DISCUSSIONS

4.1 Personal air samples

Table 4 shows the comparison of means of concentrations of total VOCs in the personal air samples among groups. We excluded one subject in the F-16 group who had fuel end up directly on the personal air monitor. The frequency of detection of total VOCs in the personal air samples were higher in the jet fuel exposed groups (95.7 - 100%) than in the control groups with the exception of CM (CJ and CK: 70.6% and 63.6%; CM: 100%). The means of concentration of the total VOCs in the personal air samples for F-4 were significantly higher than the other groups except for F-15, T-4. The means for F-15 were significantly higher than CJ and CK and F-16 was significantly higher than CK. For the total VOCs in the personal air samples, T-4, F-4 and F-15 were significantly higher than the control group of same AB (For T-4 and F-4, compared with CJ).

Table 4. Comparison of VOC concentrations in personal air samples

Groups		Control			Jet fuel exposure				
		CJ	CK	CM	T-4	F-2	F-4	F-15	F-16
Number		34	22	15	29	7	20	23	17
Fuel		N/A			JetA1		JP-4	JP-8	
Frequency (%)		70.6	63.6	100	96.6	100	100	95.7	100
Means±SEM (ppb)		3.1±0.6	15.1±10.0	4.7±1.8	14.4±2.4	2.8±0.5	116.1±47.5	229.6±122.7	10.9±3.4
Control	CJ		n.s.	n.s.	**T-4>**	n.s.	**F-4>**	**F-15>**	n.s.
	CK	n.s.		**CM>**	**T-4>**	n.s.	**F-4>**	**F-15>**	**F-16>**
	CM	n.s.	**CM>**		n.s.	n.s.	**F-4>**	n.s.	n.s.
Jet fuel exposure	T-4	**T-4>**	**T-4>**	n.s.			**F-4>**	n.s.	n.s.
	F-2	n.s.	n.s.	n.s.	n.s.		**F-4>**	n.s.	n.s.
	F-4	**F-4>**	**F-4>**	**F-4>**	**F-4>**	**F-4>**		n.s.	**F-4>**
	F-15	**F-15>**	**F-15>**	n.s.	n.s.	n.s.	n.s.		n.s.
	F-16	n.s.	**F16>**	n.s.	n.s.	n.s.	**F-4>**	n.s.	

Abbreviations: ppb, parts per billion. SEM, standard error of the mean. n.s, Not Significant. Bold font and squares highlighted in yellow indicate statistically significant difference.

Table 5 showed permissible exposure limits (PELs) of VOCs concentrations in the workplace environment as recommended by the Japan Society for Occupational Health (JSOH: 2022) and the Occupational Safety and Health Administration (OSHA: 2022). These PELs are judged to show no adverse health effects if the average exposure concentration of the hazardous substance is below this value when workers are exposed to the hazardous substance for 8 hours a day, 40 hours a week, at a less physically demanding work intensity.
The PELs in Table 5 are for the substance when it is present in air on its own. The toxicity of two or more substances is assumed to be additive and an exposure exceeding the PELs is considered to have occurred if the value of *I*, calculated according to the following formula, exceeds 1.

$$I = C_1/T_1 + C_2/T_2 + \ldots C_i/T_i + \ldots C_n/T_n$$

Ci = average exposure concentration of each component
Ti = the permitted concentration of each component

The calculated values (*I*) by JSOH and OSHA for each group according to the above formula are as follows: CJ (JSOH: 7×10^{-5}; OSHA: 2×10^{-5}), CK (1×10^{-5}; $<1 \times 10^{-5}$), CM(1×10^{-4}; 2×10^{-4}), T-4 (1×10^{-4}; 7×10^{-5}), F-2 (4×10^{-5}; 1×10^{-5}), F-4 (2×10^{-3}; 8×10^{-3}), F-15 (1×10^{-3}; 5×10^{-4}) and F-16 (1×10^{-4}; 2×10^{-4}). The total VOCs in the personal air samples in each group were extremely low compared to these recommended limits. Such trace amounts of VOCs are also known to occur in carpet and wallpaper adhesives and can be detected in office and home environments.

Table 5. Permissible exposure limits of VOCs

VOCs (ppm)	Japan Society for Occupational Health (JSOH: 2022)	Occupational Safety and Health Administration (OSHA: 2022)
n-Hexane	40	500
n-Heptane	200	500
n-Octane	300	-
n-Nonane	200	-
n-Decane	-	-
n-Undecane	-	
n-Dodecane	-	-
n-Tridecane	-	-
n-Tetradecane	-	-
n-Pentadecane	-	-
Benzene	-	1
Toluene	50	200
Ethylbenzene	20	100
Xylene (o-,m-,p- isomers)	50	100

Table 6 shows the frequency of detection of and the means of concentrations of the components of VOCs in the personal air samples. The flight line personnel for the F-4 and F-15 were exposed to relatively higher levels of chemicals more frequently, highlighting the cells that shows the frequency of detection of VOC > 60% and the means of concentrations of VOC > 1.0 ppb in the personal air samples. Differences in the components of VOCs in the personal air samples were observed between each jet fuel exposure group. The differences in the components of VOCs in the air samples between JP-4, JetA1 and JP-8 in each type of aircraft were considered as corresponding to each fuel composition. JP-4 primarily consist of C4 to C16 hydrocarbons and JP-8 and JetA1 primarily consist of C9 to C16 hydrocarbons. In addition, JP-8, which is in the kerosene class, has less benzene and n-hexane than JP-4, which is a wider cut of aromatics.

Table 6. Frequency of detection and means of VOC concentrations in personal air samples

	Control			Jet fuel exposure				
	CJ	CK	CM	T-4	F-2	F-4	F-15	F-16
Number	34	22	15	29	7	20	23	17
Fuel	N/A			JetA1		JP-4	JP-8	
Straight chain alkanes								
n-Hexane (%)	35.3	0	33.3	6.9	57.1	**100**	13.0	35.3
Means±SEM	0.14±0.04	0	0.88±0.56	0.14±0.10	0.37±0.14	**36.55±20.36**	0.89±0.51	0.43±0.18
n-Heptane (%)	5.9	4.5	6.7	20.7	28.6	**100**	56.5	35.3
Means±SEM	0.11±0.10	0.01±0.01	0.09±0.09	3.74±1.60	0.15±0.10	**21.41±8.43**	3.04±1.89	0.47±0.24
n-Octane (%)	5.9	0	0	27.6	28.6	**90.0**	**87.0**	35.3
Means±SEM	0.09±0.08	0	0	0.43±0.15	0.14±0.09	**9.07±3.61**	**8.71±5.76**	0.55±0.30
n-Nonane (%)	14.7	27.3	0	**72.4**	**71.4**	**85.0**	**91.3**	58.8
Means±SEM	0.08±0.03	0.07±0.02	0	**1.58±0.31**	**0.40±0.11**	**4.84±2.19**	**42.81±26.19**	1.70±0.74
n-Decane (%)	20.6	13.6	0	**89.7**	**85.7**	**65.0**	**91.3**	**82.4**
Means±SEM	0.29±0.12	0.15±0.10	0	**1.98±0.31**	**0.34±0.06**	**3.26±1.82**	**58.59±32.09**	**1.33±0.49**
n-Undecane (%)	8.8	13.6	6.7	**82.8**	0	55.0	**91.3**	70.6
Means±SEM	0.03±0.02	1.40±1.01	0.01±0.01	**1.57±0.23**	0	2.70±1.78	**46.87±25.26**	0.82±0.28
n-Dodecane (%)	0	22.7	13.3	**62.1**	0	55.0	**91.3**	82.4
Means±SEM	0	4.31±3.05	0.02±0.02	**0.94±0.17**	0	2.32±1.72	**26.94±14.82**	0.61±0.19
n-Tridecane (%)	0	36.4	13.3	34.5	0	25.0	**95.7**	76.5
Means±SEM	0	5.00±3.41	0.03±0.02	0.38±0.11	0	1.55±1.42	**13.03±7.38**	0.48±0.12
n-Tetradecane (%)	14.7	36.4	26.7	0	0	10.0	**91.3**	82.4
Means±SEM	0.03±0.01	2.66±1.83	0.06±0.03	0	0	0.97±0.93	**4.62±2.59**	0.40±0.12
n-Pentadecane (%)	0	13.6	6.7	3.4	0	10.0	47.8	41.2
Means±SEM	0	1.09±0.82	0.01±0.01	0.05±0.05	0	0.40±0.39	1.11±0.60	0.18±0.11
Aromatic hydrocarbons								
Benzene (%)	0	0	40.0	3.4	0	**95.0**	26.1	29.4
Means±SEM	0	0	0.23±0.11	0.04±0.04	0	**7.67±4.28**	0.25±0.14	0.13±0.05
Toluene (%)	**67.6**	50.0	**100**	**75.9**	85.7	**100**	**91.3**	**88.2**
Means±SEM	**1.19±0.20**	0.36±0.15	**2.58±0.90**	**2.14±0.46**	0.93±0.19	**13.28±4.54**	**2.05±1.06**	**1.27±0.32**
Ethylbenzene (%)	47.1	0	40.0	3.4	0	**60.0**	56.5	41.2
Means±SEM	0.46±0.11	0	0.25±0.09	0.07±0.07	0	**2.10±0.83**	2.42±1.65	0.29±0.13
m,p-Xylene (%)	47.1	0	80.0	51.7	71.4	**90.0**	**91.3**	**94.1**
Means±SEM	0.45±0.11	0	0.05±0.12	1.04±0.23	0.49±0.13	**8.34±3.21**	**16.75±10.60**	**1.58±0.48**
o-Xylene (%)	35.3	9.1	13.3	41.4	0	**80.0**	**87.0**	58.8
Means±SEM	0.18±0.05	0.02±0.01	0.06±0.05	0.27±0.06	0	**1.60±0.64**	**1.48±0.71**	0.70±0.36

Abbreviations: SEM, standard error of the mean. Bold font and squares highlighted in yellow indicate that the frequency of detection of VOC >60% and the means of concentrations of VOC >1.0 ppb.

4.2 Blood

Table 7 shows the comparison of concentrations of total VOCs in the blood among groups. We removed the blood drawn in one subject in the F-15 group who elicited a vagus reflex. The frequency of detection of total VOCs in blood were 100% for all groups. In the means of concentration of the total VOCs in blood samples, F-4 was significantly higher than the other groups except for F-2 and F-15. The means for F-15 were significantly higher than CJ, CM, T-4 and F-16. F-16 was significantly higher than T-4. Only F-4 was significantly higher than the control group of same AB (For F-4, compared with CJ).

Table 7. Comparison of VOC concentrations in blood

Groups		Control			Jet fuel exposure				
		CJ	CK	CM	T-4	F-2	F-4	F-15	F-16
Number		34	22	15	29	7	20	22	18
Fuel		N/A			JetA1		JP-4	JP-8	
Frequency (%)		100	100	100	100	100	100	100	100
Means ± SEM (ng/mL)		1.32±0.21	2.27±0.19	1.02±0.06	0.66±0.31	0.85±0.52	4.31±0.53	2.26±0.30	1.23±0.17
Control	CJ		n.s.	n.s.	n.s.	n.s.	**F-4>**	**F-15>**	n.s.
	CK	n.s.		**CK>**	**CK>**	n.s.	**F-4>**	n.s.	**CK>**
	CM	n.s.	**CK>**		**CM>**	n.s.	**F-4>**	**F-15>**	n.s.
Jet fuel exposure	T-4	n.s.	**CK>**	**CM>**		n.s.	**F-4>**	**F-15>.**	**F-16>**
	F-2	n.s.	n.s.	n.s.	n.s.		n.s.	n.s.	n.s.
	F-4	**F-4>**	**F-4>**	**F-4>**	**F-4>**	n.s.		n.s.	**F-4>**
	F-15	**F-15>**	n.s.	**F-15>**	**F-15>**	n.s.	n.s.		**F-15>**
	F-16	n.s.	**CK>**	n.s.	**F-16>**	n.s.	**F-4>**	**F-15>**	

Abbreviations: ng, nanograms. SEM, standard error of the mean. n.s, Not Significant. Bold font and squares highlighted in yellow indicate statistically significant difference.

Table 8 shows the frequency of detection and the concentrations of the components of VOCs in the blood. The frequency of detection of VOC >60% and the concentrations of VOC >0.1 ng/mL in blood were as follows: Toluene in CJ, n-Heptane, n-Octane, n-Undecane, n-Dodecane, n-Tridecane, n-Tetradecane, n-Pentadecane, Toluene and Ethylbenzene in CK, n-Dodecane, n-Tridecane, n-Tetradecane, n-Pentadecane and Toluene in CM, n-Nonane and Toluene in T-4, Toluene in F-2, n-Hexane, n-Heptane, n-Octane, n-Nonane, n-Undecane, n-Dodecane, n-Tridecane, n-Tetradecane, n-Pentadecane, Benzene, Toluene and Ethylbenzene in F-4, n-Heptane, n-Octane, n-Undecane, n-Dodecane, n-Tridecane, n-Tetradecane, Toluene and Ethylbenzene in F-15 and n-Dodecane, n-Tetradecane and Toluene in F-16. Toluene was detected in all groups. Differences were observed between the jet fuel exposure groups for the components of VOCs in the blood as well as in the personal air samples. Again the differences may be due to differences in the composition of the respective jet fuels and the performance of the respective jet engines. On the other hand, some components of VOCs in the blood were also found at a high frequency of detection and with concentrations similar to or lower than in the control groups, CK and CM. Toluene was found 100% in CJ with a concentration higher than T4 but less than F-2. It is possible that these control levels do not reflect VOCs in the work environment.

Table 8. Frequency of detection and means of VOC concentrations in blood

	Control			Jet fuel exposure				
	CJ	CK	CM	T-4	F-2	F-4	F-15	F-16
Number	34	22	15	29	7	20	22	18
Fuel	N/A			JetA1		JP-4	JP-8	
Straight chain alkanes								
n-Hexane (%)	8.8	68.2	6.7	6.9	14.3	**70.0**	59.1	11.1
Means±SEM	0.02±0.01	0.07±0.02	0	0.05±0.05	0.01±0.01	**0.31±0.08**	0.10±0.03	0.15±0.15
n-Heptane (%)	20.6	**90.9**	0	27.6	0	**85.0**	**100**	0
Means±SEM	0.07±0.03	**0.24±0.07**	0	0.03±0.01	0	**0.36±0.16**	**0.39±0.13**	0
n-Octane (%)	41.2	**77.3**	13.3	10.3	14.3	**95.0**	**100**	11.1
Means±SEM	0.12±0.04	**0.23±0.07**	0	0.01±0.01	0.01±0.01	**0.45±0.18**	**0.39±0.13**	0.01±0.01
n-Nonane (%)	5.9	40.9	0	**93.1**	100	**95.0**	95.5	11.1
Means±SEM	0.01±0.01	0.02±0.01	0	**0.11±0.02**	0.07±0.01	**0.11±0.02**	0.07±0.01	0.01±0
n-Decane (%)	0	0	0	0	0	5.0	0	0
Means±SEM	0	0	0	0	0	0.01±0.01	0	0
n-Undecane (%)	47.1	**100**	66.7	69.0	57.1	**85.0**	**100**	5.6
Means±SEM	0.08±0.02	**0.11±0.01**	0.07±0.02	0.05±0.01	0.07±0.04	**0.10±0.02**	**0.11±0.01**	0.00±0.00
n-Dodecane (%)	50.0	**100**	**93.3**	24.1	14.3	**100**	**100**	**100**
Means±SEM	0.11±0.02	**0.20±0.01**	**0.11±0.01**	0.02±0.01	0.03±0.03	**0.17±0.02**	**0.19±0.01**	**0.10±0.01**
n-Tridecane (%)	50.0	**100**	**100**	20.7	14.3	**100**	**100**	100
Means±SEM	0.16±0.03	**0.40±0.04**	**0.08±0.01**	0.02±0.01	0.01±0.01	**0.34±0.04**	**0.36±0.05**	0.07±0.01
n-Tetradecane (%)	50.0	**95.5**	**100**	6.9	14.3	**100**	**100**	**100**
Means±SEM	0.23±0.05	**0.29±0.03**	**0.19±0.01**	0.01±0.01	0.02±0.02	**0.58±0.08**	**0.24±0.03**	**0.20±0.01**
n-Pentadecane (%)	35.3	**86.4**	**100**	10.3	0	**100**	54.5	100
Means±SEM	0.03±0.01	**0.05±0.01**	**0.08±0.01**	0.01±0.01	0	**0.13±0.02**	0.04±0.01	0.09±0.01
Aromatic hydrocarbons								
Benzene (%)	26.5	40.9	46.7	10.3	28.6	**60.0**	59.1	11.1
Means±SEM	0.02±0.01	0.03±0.01	0.04±0.02	0.01±0.01	0.04±0.03	**0.32±0.11**	0.07±0.02	0.01±0.01
Toluene (%)	**100**	**100**	**100**	**96.6**	**100**	**100**	**100**	**100**
Means±SEM	**0.36±0.04**	**0.47±0.01**	**0.42±0.04**	**0.15±0.03**	**0.48±0.26**	**0.81±0.06**	**0.48±0.01**	**0.51±0.04**
Ethylbenzene (%)	55.9	**100**	20.0	3.4	14.3	**100**	**100**	83.3
Means±SEM	0.08±0.02	**0.14±0.01**	0.01±0.01	0.04±0.04	0.05±0.05	**0.54±0.18**	**0.15±0.01**	0.08±0.01
m,p-Xylene (%)	2.9	4.5	0	3.4	14.3	10.0	4.5	0
Means±SEM	0.01±0.01	0.00±0.00	0	0.11±0.11	0.05±0.05	0.02±0.02	0.00±0.00	0
o-Xylene (%)	41.2	18.2	0	3.4	14.3	90.0	31.8	38.9
Means±SEM	0.03±0.01	0.01±0	0	0.05±0.05	0.02±0.02	0.07±0.01	0.01±0	0.01±0

Abbreviations: SEM, standard error of the mean. Bold font and squares highlighted in yellow indicate that the frequency of detection of VOC >60% and concentrations of VOC >0.1 ng/mL.

4.3 Urine prior to shift

Table 9 shows the comparison of concentrations of total VOCs in the urine prior to shift among groups. The frequency of detection of total VOCs in the urine prior to shift were higher in the jet fuel exposed groups (94.4 - 100%) than in the control groups with the exception of CM (CJ and CK: 76.5% and 86.4%; CM: 100%). For the concentration of the total VOCs in the urine prior to shift, the T-4 group was significantly higher than CM and F-4 while F-15 was significantly higher than CJ, CM, T-4 and F-16. Only F-4 was significantly higher than the control group of the same AB (For F-4, compared with CJ).

Table 9. Comparison of concentrations of total VOCs in urine prior to shift

Groups		Control			Jet fuel exposure				
		CJ	CK	CM	T-4	F-2	F-4	F-15	F-16
Number		34	22	15	29	7	20	23	18
Fuel		N/A			JetA1		JP-4	JP-8	
Frequency (%)		76.5	86.4	100	100	100	100	100	94.4
Means ± SEM (ng/100μ g Cr)		0.059±0.032	0.074±0.016	0.012±0.003	0.037±0.007	0.045±0.011	0.232±0.074	0.152±0.026	0.019±0.004
Control	CJ		n.s.	n.s.	n.s.	n.s.	**F-4>**	**F-15>**	n.s.
	CK	n.s.		n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
	CM	n.s.	n.s.		**T-4>**	n.s.	**F-4>**	**F-15>**	n.s.
Jet fuel exposure	T-4	n.s.	n.s.	**T-4>**		n.s.	**F-4>**	**F-15>**	n.s.
	F-2	n.s.	n.s.	n.s.	n.s.		n.s.	n.s.	n.s.
	F-4	**F-4>**	n.s.	**F-4>**	**F-4>**	n.s.		n.s.	**F-4>**
	F-15	**F-15>**	n.s.	**F-15>**	**F-15>**	n.s.	n.s.		**F-15>**
	F-16	n.s.	n.s.	n.s.	n.s.	n.s.	**F-4>**	**F-15>**	

Abbreviations: SEM, standard error of the mean. n.s, Not Significant. Cr, creatinine. Bold font and squares highlighted in yellow indicate statistically significant difference.

Table 10 showed the frequency of detection of and the concentrations of the components of VOCs in the urine prior to shift. The frequency of detection of VOCs >60% and the concentration of VOC >0.1 ng/100 μg Cr in the urine prior to shift was only seen for Benzene in F-4.

Table 10. Frequency of detection and means of VOC concentrations in urine prior to shift

	Control			Jet fuel exposure				
	CJ	CK	CM	T-4	F-2	F-4	F-15	F-16
Number	34	22	15	29	7	20	23	18
Fuel	N/A			JetA1		JP-4	JP-8	
Straight chain alkanes								
n-Hexane (%)	0	4.5	0	0	0	10.0	0	0
Means±SEM	0	0.001±0.001	0	0	0	0.002±0.001	0	0
n-Heptane (%)	0	0	6.7	37.9	0	0	21.7	0
Means±SEM	0	0	0.001±0.001	0.005±0.002	0	0	0.009±0.004	0
n-Octane (%)	0	0	0	0	0	0	0	0
Means±SEM	0	0	0	0	0	0	0	0
n-Nonane (%)	0	0	0	6.9	0	0	0	0
Means±SEM	0	0	0	0.000±0.000	0	0	0	0
n-Decane (%)	0	0	0	0	0	0	0	0
Means±SEM	0	0	0	0	0	0	0	0
n-Undecane (%)	0	4.5	40.0	69.0	0	10.0	0	0
Means±SEM	0	0.000±0.000	0.001±0.000	0.003±0.001	0	0.006±0.005	0	0
n-Dodecane (%)	8.8	9.1	0	10.3	0	20.0	26.1	0
Means±SEM	0.001±0.001	0.001±0.001	0	0.000±0.000	0	0.001±0.001	0.003±0.001	0
n-Tridecane (%)	0	13.6	0	31.0	42.9	0	47.8	0
Means±SEM	0	0.001±0.000	0	0.001±0.001	0.005±0.003	0	0.004±0.001	0
n-Tetradecane (%)	0	13.6	6.7	24.1	57.1	0	0	0
Means±SEM	0	0.004±0.003	0.000±0.000	0.004±0.002	0.011±0.005	0	0	0
n-Pentadecane (%)	0	45.5	6.7	44.8	85.7	10.0	13.0	0
Means±SEM	0	0.004±0.001	0.000±0.000	0.006±0.002	0.015±0.004	0.001±0.001	0.002±0.001	0
Aromatic hydrocarbons								
Benzene (%)	26.5	50.0	60.0	6.9	28.6	**85.0**	43.5	83.3
Means±SEM	0.039±0.028	0.033±0.010	0.004±0.002	0.001±0.001	0.006±0.004	**0.179±0.074**	0.035±0.016	0.010±0.002
Toluene (%)	67.6	72.7	80.0	48.3	57.1	95.0	100	83.3
Means±SEM	0.019±0.005	0.031±0.010	0.006±0.001	0.014±0.004	0.009±0.004	0.044±0.007	0.099±0.014	0.009±0.002
Ethylbenzene (%)	2.9	0	6.7	17.2	0	0	0	5.6
Means±SEM	0.000±0.000	0	0.000±0.000	0.002±0.001	0	0	0	0.000±0.000
m,p-Xylene (%)	0	0	0	0	0	0	0	0
Means±SEM	0	0	0	0	0	0	0	0
o-Xylene (%)	2.9	0	0	3.4	0	0	0	0
Means±SEM	0.000±0.000	0	0	0.000±0.000	0	0	0	0

Abbreviations: SEM, standard error of the mean. Cr, creatinine. Bold font and squares highlighted in yellow indicate that the frequency of detection of VOC >60% and concentrations of VOC >0.1 ng/100µg Cr.

4.4 Urine post shift

Table 11 shows the comparison of concentrations of total VOCs in the urine post shift among groups. The volume of urine post shift required for analysis could not be collected for two subjects in the F-4 group. The frequency of detection of total VOCs in the urine post shift were as follows: the control groups (79.4 - 93.3%) and the jet fuel exposed groups (85.7 - 100%). For the concentration of the total VOCs in the urine post shift, T-4 was significantly higher than CM and F-16 while F-4 was significantly higher than CJ, CM, T-4 and F-16. The F-15 group was significantly higher than CM and F-16. Only F-4 was significantly higher than the control group of same AB (For F-4, compared with CJ).

Table 11. Comparison of VOC concentrations in urine post shift

Groups		Control			Jet fuel exposure				
		CJ	CK	CM	T-4	F-2	F-4	F-15	F-16
Number		34	22	15	29	7	18	23	18
Fuel		N/A			JetA1		JP-4	JP-8	
Frequency (%)		79.4	81.8	93.3	100	85.7	100	95.7	94.4
Means ± SEM (ng/100μ g Cr)		0.076±0.020	0.097±0.030	0.015±0.006	0.067±0.008	0.070±0.021	0.285±0.081	0.266±0.106	0.018±0.004
Control	CJ		n.s.	n.s.	n.s.	n.s.	**F-4>**	n.s.	n.s.
	CK	n.s.		n.s.	n.s.	n.s.	n.s.	n.s.	n.s.
	CM	n.s.	n.s.		**T-4>**	n.s.	**F-4>**	**F-15>**	n.s.
Jet fuel exposure	T-4	n.s.	n.s.	**T-4>**		n.s.	**F-4>**	n.s.	**T-4>**
	F-2	n.s.	n.s.	n.s.	n.s.		n.s.	n.s.	n.s.
	F-4	**F-4>**	n.s.	**F-4>**	**F-4>**	n.s.		n.s.	**F-4>**
	F-15	n.s.	n.s.	**F-15>**	n.s.	n.s.	n.s.		**F-15>**
	F-16	n.s.	n.s.	n.s.	**T-4>**	n.s.	**F-4>**	**F-15>**	

Abbreviations: SEM, standard error of the mean. n.s, Not Significant. Cr, creatinine. Bold font and squares highlighted in yellow indicate statistically significant difference.

Table 12 shows the frequency of detection of and the concentrations of the components of VOCs in the urine post shift. The frequency of detection of VOC >60% and the concentrations of VOC >0.1 ng/100μg Cr in the urine prior to shift was only seen for Benzene in the F-4 group and Toluene in the F-15 group. Benzene was found at high frequencies and concentrations in the personal air samples, the blood, urine prior to shift and urine post shift for the F-4 group.

Table 12. Frequency of detection and means of VOC concentrations in urine post shift

	Control			Jet fuel exposure				
	CJ	CK	CM	T-4	F-2	F-4	F-15	F-16
Number	34	22	15	29	7	18	23	18
Fuel	N/A			JetA1		JP-4	JP-8	
Straight chain alkanes								
n-Hexane (%)	8.8	0	0	13.8	0	50.0	13.0	0
Means±SEM	0.001±0.001	0	0	0.002±0.001	0	0.008±0.003	0.002±0.001	0
n-Heptane (%)	0	0	0	75.9	0	0	0	0
Means±SEM	0	0	0	0.013±0.002	0	0	0	0
n-Octane (%)	0	0	0	20.7	0	0	0	0
Means±SEM	0	0	0	0.002±0.001	0	0	0	0
n-Nonane (%)	0	0	0	24.1	0	0	4.3	0
Means±SEM	0	0	0	0.001±0.001	0	0	0.001±0.001	0
n-Decane (%)	0	0	0	0	0	0	0	0
Means±SEM	0	0	0	0	0	0	0	0
n-Undecane (%)	0	4.5	53.3	55.2	42.9	27.8	4.3	11.1
Means±SEM	0	0.000±0.000	0.002±0.001	0.006±0.001	0.13±0.009	0.002±0.001	0.001±0.001	0.000±0.000
n-Dodecane (%)	17.6	22.7	0	6.9	0	22.2	47.8	0
Means±SEM	0.003±0.002	0.007±0.004	0	0.001±0.001	0	0.005±0.003	0.008±0.003	0
n-Tridecane (%)	0	36.4	0	41.4	57.1	5.6	43.5	55.6
Means±SEM	0	0.003±0.001	0	0.005±0.001	0.011±0.006	0.001±0.001	0.003±0.001	0.001±0.000
n-Tetradecane (%)	0	13.6	6.7	89.7	71.4	11.1	4.3	27.8
Means±SEM	0	0.008±0.005	0.001±0.001	0.017±0.003	0.027±0.010	0.002±.0.002	0.001±0.001	0.001±0.000
n-Pentadecane (%)	0	40.9	0	82.8	28.6	0	4.3	5.6
Means±SEM	0	0.016±0.008	0	0.012±0.012	0.011±0.008	0	0.001±0.001	0.000±0.000
Aromatic hydrocarbons								
Benzene (%)	47.1	50.0	26.7	6.9	28.6	**100**	30.4	33.3
Means±SEM	0.040±0.016	0.013±0.005	0.004±0.003	0.003±0.002	0.007±0.004	**0.201±0.66**	0.124±0.084	0.006±0.003
Toluene (%)	76.5	68.2	53.3	20.7	14.3	100	**91.3**	88.9
Means±SEM	0.027±0.005	0.048±0.018	0.004±0.001	0.005±0.002	0.001±0.001	0.061±0.011	**0.125±0.029**	0.009±0.002
Ethylbenzene (%)	17.6	4.5	6.7	0	0	5.6	0	11.1
Means±SEM	0.004±0.002	0.001±0.001	0.003±0.003	0	0	0.000±0.000	0	0.001±0.000
m,p-Xylene (%)	0	0	6.7	0	0	5.6	0	0
Means±SEM	0	0	0.001±0.001	0	0	0.005±0.005	0	0
o-Xylene (%)	11.8	0	6.7	0	14.3	0	0	16.7
Means±SEM	0.001±0.001	0	0.001±0.001	0	0.001±0.001	0	0	0.000±0.000

Abbreviations: SEM, standard error of the mean. Cr, creatinine. Bold font and squares highlighted in yellow indicate that the frequency of detection of VOC >60% and concentrations of VOC >0.1 ng/100µg Cr.

4.5 Comparison of VOCs in urine prior to and post shift

Figure 3 showed comparison of concentrations for the total of VOCs in the urine prior to and post shift. The volume of urine post shift required for analysis could not be collected for two subjects in the F-4 group. Total VOCs concentrations in urine samples were significantly higher post shift than prior to shift in CJ and T-4 group, but not significantly different in the other groups.

It is known that the air-urinary metabolites relationships of VOCs are influenced by age, gender, race/ethnicity, and smoking habits (Jain, 2010). Although this study measures VOCs in urine rather than urinary metabolites of VOCs and therefore cannot be generalized, the differences observed only in CJ and T-4 might have been influenced by race/ethnicity as well as fuel type and engine performance.

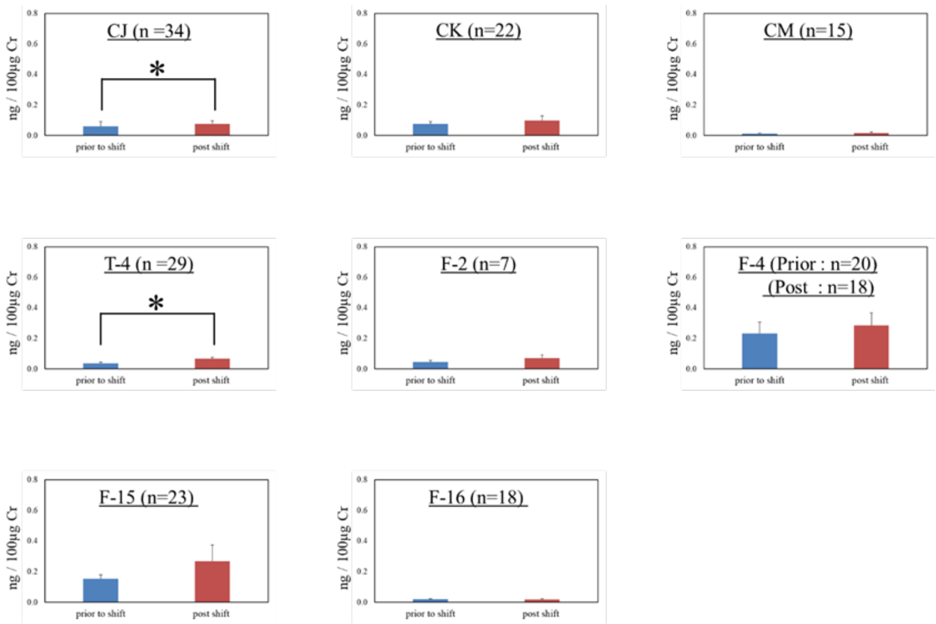
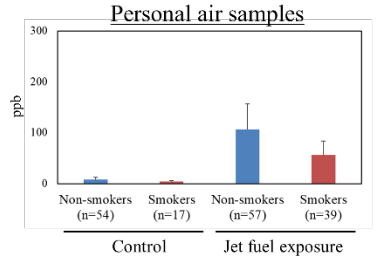


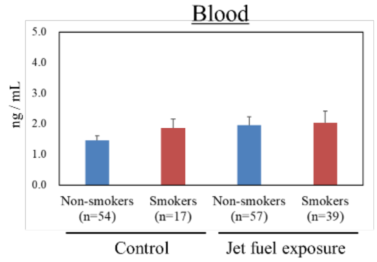
Figure 3: Comparison of VOC concentrations in urine prior to and post shift
Abbreviations: SEM, standard error of the mean. Cr, creatinine. Asterisk indicate statistically significant difference.

4.6 Comparison of VOCs in blood and urine in smokers and non-smokers

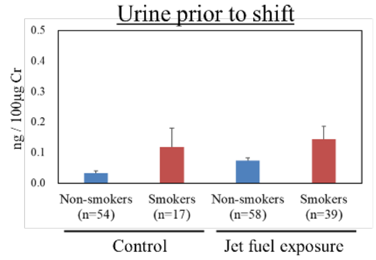
Tobacco smoke contains more than 8,000 chemicals, including VOCs (De Jesús VR et al., 2020). For this reason, we compared to the total VOCs in the personal air samples, the blood, the urine prior to shift and the urine post shift in smokers and non-smokers. Figure 4 shows the comparison of the total VOCs in the blood, the urine prior to and post shift in smokers and non-smokers. The subjects were divided into four groups: NC, Non-smokers in control subjects; SC, Smokers in control subjects; NE, Non-smokers in jet fuel exposed subjects and SE, Smokers in jet fuel exposed subjects. The air-blood and air-urinary metabolites relationship of VOCs is known to be affected by smoking habits, age and gender (Lin, Egeghy and Rappaport, 2008; Jain, 2010). The VOCs in the urine prior to shift and post shift for the NE and SE groups were significantly higher than in NC. These results might be attributed to high VOC concentrations in the personal air samples of NE and SE. On the other hand, no significant differences were found between NC and SC and NE and SE for total VOCs in the personal air samples, the blood, and urine prior to shift and post shift. In this study, the smoking habits had no effect on VOCs in blood, the urine prior to shift and post shift, and no interaction effect between exposure to VOCs and smoking habits. Moreover, we examined the relationship between VOCs and the questionnaire survey items, Years of service, Age, Gender and Hobbies, but found no association.



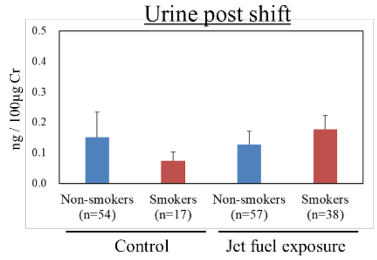
	NC	SC	NE	SE
NC		n,.s.	**NE >**	**SE >**
SC	n,.s.		**NE >**	**SE >**
NE	**NE >**	**NE >**		n,.s.
SE	**SE >**	**SE >**	n,.s.	



	NC	SC	NE	SE
NC		n,.s.	n,.s.	n,.s.
SC	n,.s.		n,.s.	n,.s.
NE	n,.s.	n,.s.		n,.s.
SE	n,.s.	n,.s.	n,.s.	



	NC	SC	NE	SE
NC		n,.s.	**NE >**	**SE >**
SC	n,.s.		n,.s.	n,.s.
NE	**NE >**	n,.s.		n,.s.
SE	**SE >**	n,.s.	n,.s.	



	NC	SC	NE	SE
NC		n,.s.	**NE >**	**SE >**
SC	n,.s.		n,.s.	n,.s.
NE	**NE >**	n,.s.		n,.s.
SE	**SE >**	n,.s.	n,.s.	

Figure 4: Comparison of the total VOCs in blood, urine prior to shift and urine post shift in smokers and non-smokers

Abbreviations: n.s, Not Significant. Bold font and squares highlighted in yellow indicate statistically significant difference.

5.0 CONCLUSIONS

The study successfully showed the characteristics of VOCs exposures in the flight line environment for each aircraft type and fuel type. Because total VOCs in the personal air samples of each group were very low compared to the acceptable limits recommended by the JSOH and OSHA, they are not considered to cause adverse health effects in the flight line personnel.

Only total VOCs of all samples (air sample, blood and urine prior to and post shift) of the F-4 group were higher than those of the control group for the same AB. For engine performance, the F-4 engine is a turbojet, while the other aircraft use turbofans. The turbofan is more prone to dilution of the combustion gases than the turbojet, as the air in the bypass stream and the combustion gases in the core stream mix at the nozzle. As a result, turbofan engines may have lower total concentrations of VOCs in their exhaust and personal air samples than turbojets, which may also be reflected in the blood and urine. JP-4 jet fuel also contains more short-chain hydrocarbons and aromatics than JetA1 and JP-8. Short-chain hydrocarbons and aromatics (such as benzene) are more volatile than long-chain hydrocarbons; therefore, they occur more in the personal air samples and are more easily absorbed from the lungs, which appears to have been reflected in the blood and urine.

Since the F-4 and JP-4 jet fuel are no longer operational in the JASDF and USAF, retiring both makes the current flight line environment safer.

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SYMBOLS, ABBREVIATIONS AND ACRONYMS

º	Degrees
%	Percent
μg	micrograms
AB	air base
ABR	auditory brain response
C	Celcius
CJ	Non-exposed control subjects in JASDF
CK	Non-exposed control subjects in Kadena
CM	Non-exposed control subjects in Misawa
Cr	creatinine
DPOAE	distortion product otoacoustic emissions
E I	electron ionization
F-2	JetA1 exposed F-2 flight line crews in Matsushima
F-4	JP-4 exposed F-4 flight line crews in Hyakuri
F-15	JP-8 exposed F-15 flight line crews in Kadena
F-16	JP-8 exposed F-16 flight line crews in Misawa.
GC-FID	Gas Chromatography-Flame Ionization Detector
GC/MS	Gas Chromatography/Mass Spectrocopy
GC/MSD	Gas Chromatography-Mass Spectrometer Detector
JASDF	Japan Air Self-Defense Force
JSOH	Japan Society for Occupational Health
mL	milliliters
NATO	North Atlantic Treaty Organization
ng	nanograms
n.s	Not Significant.
OAE	otoacoustic emissions
OSHA	Occupational Safety and Health Administration
PELs	permissible exposure limits
ppb	part per billion
μL	microliters
USAF	US Air Force
SEM	standard error of the mean.
T-4	JetA1 exposed T-4 flight line crews in Matsushima and Hamamatsu
VOCs	volatile organic compounds