'14

前期日程

受験番号 見本

医学部医学科小論文問題

注　意　事　項

1. 試験開始の合図があるまで問題冊子を開いてはいけません。
2. この問題冊子のページ数は6ページです。問題冊子，答案用紙(3枚)及び下書き用紙(3枚)に落丁，乱丁，印刷不鮮明などがある場合には申し出てください。
3. 問題を解くに当たっては，「訳注一覧」が問題冊子に挿入されていますので，取り外して使用してください。
4. 解答は指定の答案用紙に記入してください。
   (1) 文字はわかりやすく，横書きで，はっきり記入してください。
   (2) 解答の字数に制限がある場合には，それを守ってください。
   (3) 訂正，挿入の語句は余白に記入しても構いません。
   (4) 英語をます目に記入するときは，問題文の指示に従ってください。なお，数字を記入する場合はます目にとらわれる必要はありません。
5. 試験時間は90分です。
6. 答案用紙は持ち帰ってはいけません。
7. 問題冊子と下書き用紙は持ち帰ってください。

◇M26(449—205)

次の文章を読んで設問Ａ～Ｆに答えなさい。なお訳注一覧に，＊のついた単語の訳注があります。

［出典：Boedeker E, Friedel G, Walles T. Sniffer dogs as part of a bimodal bionic research approach to develop a lung cancer screening. Interact Cardiovasc Thorac Surg. 2012 May; 14 (5): 511-5. (一部抜粋)］

Lung cancer (LC) represents the second most frequent cancer in men and women with more than 390, 000 cases/year in Europe. Among all solid cancers, it is the most common cause of death with an estimated 342, 000 deaths/year. The prognosis* of LC largely depends on disease discovery at an early stage, when the tumour* is still localized. Unfortunately, early LC is not associated with symptoms*, and detection therefore is often by chance. Clinical practice has shown that the available diagnostic* techniques (such as the various imaging technologies or bronchoscopy* including interventional biopsy* procedures) have limitations in reliably discriminating* between cancer patients and healthy subjects. Very recently, the US American National Lung Screening* Trial (NLST), a randomized* national trial involving more than 53, 000 current and former heavy smokers aged 55-74 years, compared the effects of two screening procedures for LC — low-dose helical* computed tomography* (CT) and standard chest X-ray* — on LC mortality* and found 20% lower risk of dying from LC in patients undergoing CT screening. (A) However, currently no screening method is accepted to test for LC.

For almost three decades, research is conducted to develop sensor arrays* and pattern recognition technologies, commonly referred to as (B) 'electronic noses' that can detect and recognize odours* and flavours. It is hypothesized that these devices* may be applicable in identifying volatile organic compounds* (VOCs) that are linked to cancers in their early stages and thereby making them potential non-invasive* and inexpensive diagnostic tools for the medical community. Since their first delineation* by Pauling *et al.** in 1971, 3, 481 different VOCs have been described in the human breath — most of them in picomolar concentrations (10^{-12} mol/l or particles per trillion*). However, the metabolic* origin of tumour-associated VOCs remains speculative. Despite important developments in 'electronic sensing' or 'e-sensing' technologies, their applicability in a clinical setting is limited due to the fact that patients are required to not smoke and to fast before breath samples can be taken. Other limiting factors are that an optimized* sample collection is necessary, that the instruments are very sensitive, the long durations for sample analysis, as well as high risks of signal interference. Finally, it has been shown that measuring VOCs with an electronic nose has not yet been standardized and the set-up significantly affects the results. Therefore, it is currently not possible to draw generally accepted conclusions.

(C—1) Offside popular research paths, the medical community's attention is every now and then drawn to the phenomenon that dogs may detect cancer in patients (Table 1). (C—2) Recently, our group substantiated in a prospective clinical double-blinded trial* the ability of specially trained sniffer* dogs to identify LC in the breath sample of patients with a sensitivity* of 71% and a specificity* of 93%. In contrast to e-sensing technologies, the analysis was rapid (<5 seconds/patient) and interference-free (no influence of smoking, diet, medication, secondary disease). Therefore, dogs seem to be more reliable to identify LC from the breath of patients than the current e-sensing devices. However, it is not clear on what basis (single component, VOC pattern?) the dogs come to a decision. Therefore, we propose a (D) bimodal* bionic research approach by combining the state-of-the-art* electronic nose technologies and dog training to identify a VOC target for LC screening.

(中略)

LC continues to represent a heavy burden for health care systems worldwide. Epidemiologic studies* predict that its role will increase in the near future. While patient prognosis is strongly associated with tumour stage and early detection of disease, no screening test exists so far. Acknowledging the existing limitations of current analytical tools, not walking along the beaten track*, may be worthwhile to identify an applicable screening test for LC.

'Bionics' (E) is the transfer of biological methods and systems found in nature to the study and design of engineering systems and modern technology. Examples for the successful transfer of technology are (i) the development of dirt*- and water-repellent* paint (coating) from the observation that the surface of the lotus flower plant* is practically unsticky for anything (the lotus effect); (ii) the hulls* of boats imitating the thick skin of dolphins; (iii) sonar, radar and medical ultrasound imaging* imitating the echolocation* of bats. The outstanding sensitivity of the canine olfactory system* has been acknowledged by using sniffer dogs in military and civilian service for the detection of a variety of odours. So, why not using them for the detection of LC?

A PubMed search* (limited to 'human species' and publications in German or English) for the terms 'sniffer dogs and cancer' (5 results), 'canine scent* detection' (13 results) and 'canine olfaction' (70 results) followed by an analysis of the identified studies ultimately provides three case reports and eight studies reporting on the phenomenon of specially trained sniffer dogs identifying solid tumours in patients (Table 1). Collectively, 449 patients with skin tumours (n=9), or bladder* (n=36), breast* (n=94), lung (n=115), prostate* (n=116), ovarian* (n=71), and other solid cancers (n=8) have been tested. (F) Unfortunately, most findings have to be questioned due to numerous limitations in the study design and data analysis. However, a recent study specifically addressed the existing shortcomings and documented a moderate sensitivity (71%) and high specificity (93%) for specially trained sniffer dogs to identify LC from a breath sample of patients. This analysis confirms the existence of a stable marker (or scent pattern) that is strongly associated with LC and independent from COPD*, but can be reliably discriminated from tobacco smoke, food odours and potential drug metabolites. Future studies of similar design are necessary to assess whether this dog indication is specific for LC or whether it is linked to the presence of any form of cancer (in the lung). To be applicable as a clinical screening test in patients with pathological* chest CT findings, it has to be tested whether sniffer dogs can discriminate benign lung lesions* from LC.

訳 注 一 覧

この「訳注一覧」は問題を解くに当たって，取り外して使用してください。

prognosis：予後，医学的経過の見通し

tumour：腫瘍

symptom：症状，徴候，症候

diagnostic：診断の

bronchoscopy：気管支鏡(検査)

interventional biopsy：生検，生体組織検査

discriminate：区別する，識別する.

screening：選別検査，検診

randomized：無作為の

helical：らせん状の

computed tomography：コンピュータ断層撮影

chest X-ray：胸部レントゲン検査

mortality：死亡率

sensor array：感知検出配列(器)

odour：臭気，悪臭

device：装置

volatile organic compound：揮発性有機化合物

non-invasive：身体的負担のない

delineation：記述

et al.：およびその他の者

trillion：兆

metabolic：代謝の

optimized：最適化された

double-blinded trial：二重盲検試験[特に医学の試験・研究で，実施している薬や治療法などの性質を，医師(観察者)からも患者からも不明にして行う方法]

sniffer：(臭いを)嗅ぐ

sensitivity：感度

specificity：特異度

> 感度 Sensitivity と特異度 Specificity
>
> スクリーニングの評価をする際などに用いられる指標。
>
> 感度 Sensitivity とは，疾患の人の何％が検査で陽性と把握できるか，を表し，
>
> 特異度 Specificity とは，疾患でない人は何％が検査で陰性となるか，を表す。
>
> 感度＝(真陽性)/(真陽性＋偽陰性)×100
>
> 特異度＝(真陰性)/(真陰性＋偽陽性)×100 となる。

bimodal：二峰性，二頂の

the state-of-the-art：最先端の

epidemiologic study：疫学研究

the beaten track：常道

dirt：汚れ，埃

lotus flower plant：ハス科の植物

ultrasound imaging：超音波検査

repellent：はねつける，はじく

hull：外殻

echolocation：反響定位(コウモリ・イルカなどが超音波によって物体の存在を測定する能力).

the canine olfactory system：犬の嗅覚系

PubMed search：米国国立生物工学情報センターが運営する，生物医学・生命科学のオンライン論文アーカイブ

scent：におい

breast：乳腺

ovarian：卵巣の

pathological：病理学的な

substrate：基質，材料

basal cell carcinoma：基底細胞がん

bladder：膀胱

prostate：前立腺

COPD：慢性閉塞性肺疾患

benign lung lesion：良性肺疾患

malignant melanoma：悪性黒色腫

prospective study：前向き研究(研究を立案，開始してから新たに生じる事象について調査する研究)

carcinoma：がん，がん腫

urine：尿

tissue specimen：組織検体

endocervical carcinoma：子宮頸がん

blood serum：血清

cystitis：膀胱炎

pet scan：陽電子放射断層撮影法

endometrial carcinoma：子宮内膜がん

vulvar cancer：外陰がん

Table 1:
Published evidence on the detection of solid tumours by specially trained sniffer dogs

Publication	Year	Type of study	Investigated tumour	Number of tested persons	Substrate*	Sensitivity	Specificity
Williams H, *et al.* Sniffer dogs in the melanoma clinic? Lancet 1989; 1: 734.	1989	Report of a single case	Malignant melanoma*	1	Direct body contact: skin	–	–
Church J, *et al.* Another sniffer dog for the clinic? Lancet 2001; 358: 930.	2001	Report of a single case	Basal cell carcinoma* of the skin	1	Direct body contact: skin	–	–
Pickel DP, *et al.* Evidence for canine olfactory detection of melanoma. Appl Anim Behav Sci 2004; 89: 107–116.	2004	Prospective study*	Malignant melanoma	7	Direct body contact: skin	82%	100%
Willis CM, *et al.* Olfactory detection of human bladder cancer by dogs: proof of principle study. BMJ 2004; 329: 712.	2004	Prospective study	Bladder cancer	36 with bladder cancer, 108 without carcinoma* (some with cystitis* etc.)	Urine*	41%	?
Welsh JS. Olfactory detection of human bladder cancer by dogs. Another cancer detected by 'pet scan*'. BMJ 2004; 329: 1286–1287.	2004	Report of a single case	Breast cancer	1	Direct body contact: breast	–	–
McCulloch M, *et al.* Diagnostic accuracy of canine scent detection in early- and late-stage lung and breast cancers. Interact Canc Ther 2006; 5: 30–9.	2006	Prospective study	LC, breast cancer (BC)	55 with LC/31 with breast cancer/83 healthy	Breath sample	LC: 99%, BC: 88%	LC: 99%, BC: 98%
Gordon RT, *et al.* The use of canines in the detection of human cancers. J Altern Complement Med 2008; 14: 61–67.	2008	Prospective study	Prostate cancer, breast cancer	62 with breast cancer/188 healthy persons, 57 with prostate cancer/186 healthy persons	Urine	No better than chance	No better than chance
Horvath G, *et al.* Human ovarian carcinomas detected by specific odor. Integr Cancer Ther 2008; 7: 76–80.	2008	Prospective study	Ovarian carcinoma	31 with ovarian carcinoma/? healthy	Tissue specimen*	100%	98%
Horvath G, *et al.* Characteristic odour in the blood reveals ovarian carcinoma. BMC Cancer 2010; 10: 643.	2010	Prospective study	Ovarian carcinoma	40 with ovarian carcinoma, 4 with endometrial carcinoma*, 2 with endocervical carcinoma*, 2 with vulvar cancer*/? healthy	Tissue specimen (T) and blood serum* (B)	T: 100%, B: 100%	T: 95%, B: 98%
Cornu JN, *et al.* Olfactory detection of prostate cancer by dogs sniffing urine: A step forward to early diagnosis. Eur Urology 2011; 59: 197–201.	2011	Prospective study	Prostate cancer	59 with prostate cancer, 49 with negative prostate biopsy	Urine	91%	91%
Ehmann R, *et al.* Canine scent detection in the diagnosis of lung cancer: revisiting a puzzling phenomenon. Eur Resp J; in press	2011	Prospective study	LC	60 with LC/110 healthy/50 with COPD	Breath sample	71%	93%

設　問

A．下線(A)に関して，そのためにどのような状況が生まれているか，その状況を改善するために何をすべきだと考えるか。筆者の考えと自らの考えを示し，答案用紙 **1—1** のA欄に日本語100字以内(句読点を含む。文中の英文略号の使用可，英語2文字＝日本語1文字で計算)で記入しなさい。

B．下線(B)“electronic noses’とは，(1)どのようなものか。(2)その応用による利点，(3)実用化への問題点，と3つにわけ，答案用紙 **1—1** のB欄に日本語で記入しなさい。

C—1．下線(C—1)に関して，Table 1に示された研究結果を比較し，Lung cancer (LC)における実践応用の可能性について，答案用紙 **1—1** のC—1欄に日本語150字以内(句読点を含む。文中の英文略号の使用可，英語2文字＝日本語1文字で計算)で記入しなさい。

C—2．下線(C—2)の記述に関し，答案用紙 **1—2** のC—2の表の空欄に症例数を入れて表を完成しなさい。(小数点以下四捨五入)

D．下線(D) bimodal bionic research approachとは，具体的にどのようなことをさすか。答案用紙 **1—2** のD欄に日本語80字以内(句読点を含む。文中の英文略号の使用可，英語2文字＝日本語1文字で計算)で記入しなさい。

E—1．下線(E)‘Bionics’とは具体例を含め，どのようなものと説明されているか。また，どのようにLung cancer (LC)に応用すればよいと筆者は考えているか，答案用紙 **1—2** のE—1欄に日本語120字以内(句読点を含む。文中の英文略号の使用可，英語2文字＝日本語1文字で計算)で記入しなさい。

E―2．下線(E)'Bionics'について，著者が記載していない他の成功例について，どのようなものがあると考えられるか。自らの考えで適切と思われる事例を2つあげ，答案用紙 **1―2** のE―2欄(1)，(2)に日本語で記入しなさい。

F―1．下線(F)に関して，著者はどのような点を問題と考えているか。答案用紙 **1―3** のF―1欄に日本語，箇条書きで5項目記入しなさい。

F―2．下線(F)に関して，F―1に記した著者の考え以外に不足していると思われる研究内容があるか。答案用紙 **1―3** のF―2欄に日本語120字以内(句読点を含む。文中の英文略号の使用可，英語2文字＝日本語1文字で計算)で記入しなさい。