CHAPTER 17 - ONCOLOGY

1 INTRODUCTION

[1.1 **Overview]**

Every pilot who has been treated for malignant disease will need an individual assessment before returning to flying. Recovery from surgery or radiotherapy should be assessed. Current curative or adjuvent chemotherapy is incompatible with certification, and recovery from the effects of these drugs will demand a period of a temporarily unfit assessment after the treatment has finished. If the pilot has recovered from the primary treatment, and, as far as is possible with available techniques, there is no sign of residual tumour, then the level of certification will depend on the likelihood of recurrent disease. This chapter of the guidance material will explore **[ ]**assessing the risk to flight safety from air crew who have received treatment for malignant disease **[ ]**.

[1.2 **Disqualifying conditions]**

[In addition to ensuring that treatment has been effective, pre-requisites for certification after treatment for malignant disease include satisfactory haematological parameters and no on-going side effects from therapy.

A history of malignant disease involving the central nervous system is disqualifying for certification.**]**

2 PRIMARY TREATMENT FOR MALIGNANT DISEASE

2.1 **Surgery**

Surgery is the commonest primary treatment for malignant disease, and is **[ ]**frequently the only treatment. A return to flying, from the purely surgical aspect, depends on the extent of the operation, and this can be conveniently broken down into minor, intermediate and major surgery. Examples of minimum times assessed as temporarily unfit for various types of surgery **[ ]**are shown in **[**Table 1**]**.

Operation	Example	Minimum time assessed as temporarily unfit
Minor	Excision of mole Lymph node biopsy	1 week
Intermediate	Orchidectomy for testicular tumour	4 weeks
Major	Hemicolectomy for carcinoma of colon	12 weeks

Table 1: Minimum periods of temporary unfitness before returning to flying after surgery.

It is stressed that these are minimum times, and any more extensive procedures, or any complications with, for example, wound healing will extend these times.

The **[**Aeromedical Section (AMS)**]**may consider earlier recertification if recovery is complete, the applicant is asymptomatic and there is a minimal risk of further complication.

2.2 Radiotherapy

[Pilots should be assessed as temporarily unfit during any course of radiotherapy.] Radiotherapy treatment for malignant disease is usually given as an intensive course. The aim of this may be curative, for example to an isolated group of lymph nodes which have proved by biopsy to contain lymphoma; or as adjuvent treatment, for example to the abdominal nodes following orchidectomy for a seminoma of the testis, on the assumption that they may contain metastatic tumour. Since most courses are intensive, there is little time to fly even if the pilot wished to, but many patients undergoing radiotherapy suffer non-specific systemic effects (tiredness, malaise and nausea) which make it inadvisable for any pilot to fly whilst receiving this treatment. Apart from physical symptoms there are often psychological effects and worries associated with radiotherapy, which, in common with chemotherapy, may also affect flying ability.

2.3 Chemotherapy

Pilots should be assessed as temporarily unfit during any treatment with chemotherapy. All these drugs are toxic to normal cells, and in particular to rapidly dividing cells in the bone marrow. During chemotherapy the patient is routinely tested for normal blood levels such as haemoglobin, and this should serve as a reminder both to the pilot and his AME that there are potential risks if he enters a hypoxic environment. A temporarily unfit assessment applies to curative chemotherapy, for example in the treatment of disseminated lymphoma, and also to adjuvent chemotherapy, for example in drugs given to prevent the possible recurrence of colorectal cancer following surgical excision. The latter treatment may extend over a prolonged period of time, and there may well be a conflict between the 'medical' advice to have the adjuvent treatment and the pilot's desire to regain a medical certificate to fly. The only exception to a temporarily unfit assessment during adjuvent treatment for malignancy is endocrine therapy. Certain adjuvent hormone and anti-hormone treatment following (for example) breast [or] prostate cancer treatment may be acceptable if there are no side effects.

[2.4 Stem cell transplantation]

It is possible to return to flying after stem cell transplantation providing there is sustained remission.

3 CERTIFICATION AFTER PRIMARY TREATMENT [ ]

3.1 Defining acceptable risk

In this discussion the assumption is made that the primary treatment (be it surgery, radiotherapy, chemotherapy or a combination) has removed all signs of tumour X measured clinically or by investigation. The risk to flight safety is now the possibility that local or metastatic recurrence will cause sudden or subtle incapacitation whilst the pilot is flying[ ].

The concept of 'acceptable risk' has been discussed elsewhere, and much work in aviation cardiology has defined ~~a~~ the current risk of incapacitation of up to 1% per year to be acceptable for two crew professional and unrestricted private flying. This can also be applied to certification after treatment for malignant disease. One difference between cardiology and oncology is that with the former, once the risk has been defined and certification achieved, the pathological condition is not likely to go away. After treatment of malignancy however, the prognosis [usually] improves with recurrence free time away from the original episode. Thus to consider the full range of certification possibilities, from no certificate to unrestricted Class 1, and including Class 2 certification for private flying, acceptable incapacitation risk levels have to be defined.

In this discussion the following annual incapacitation risks will be used to define the appropriate certification. It should be noted that the exact levels for restricted Class 2 certification (private flying with a safety pilot) have never been defined. [For single crew professional flying a figure of 0.1% has been empirically quoted and is a reasonable basis given that it is an order of magnitude less than the maximal acceptable multicrew figure and is the approximate cardiovascular risk of men in their 40s (Table 2).**]** For the purposes of these calculations a **[**5%**]** annual incapacitation risk has been taken as the upper limit **[**for restricted private flying**]**.

Risk per year of incapacitation	Acceptable level of certification	Licence
Less than 0·1%	Any	Any
Between 0·1% and 1%	Class 1 restricted (‘OML’) Class 2 unrestricted	2 crew professional Solo private
Greater than 1%	No Class 1 Possible Class 2 restricted (‘OSL’)	No professional Private with ‘Safety Pilot’

Table 2: Certification possibilities according to acceptable risks of incapacitation

Thus if an incapacitation rate per year can be derived for tumour X at any particular time away from its original treatment, then an acceptable level of certification for that pilot, at that time, can be calculated from the table above.

Following ‘successful’ primary treatment, the risk that tumour X will cause a subtle or sudden incapacitation depends on two factors. The first is the actual risk of recurrence, which will depend on the pathological stage of the tumour or its TNM classification (Tumour Node Metastasis). The second is the site of that recurrence, and this will depend on the primary tumour type. These two factors will now be discussed individually, again in relation to a hypothetical tumour X.

3.2 **Defining the risk of recurrence**

The annual recurrence rate of tumour X can be calculated from survival curves. Ideally these should be ‘recurrence free’ survival curves, but those are often not available, and thus simple survival data will need to be used. However, unless it is possible to cure many patients once their tumour has recurred (not a common situation) then the two curves will be very similar in shape. **[**Figure 1**]** shows a hypothetical five year survival curve for tumour X, and is used to show the usual representation of this type of data. It includes percentage figures along the curve showing the recurrence rates for each of the five years following treatment.

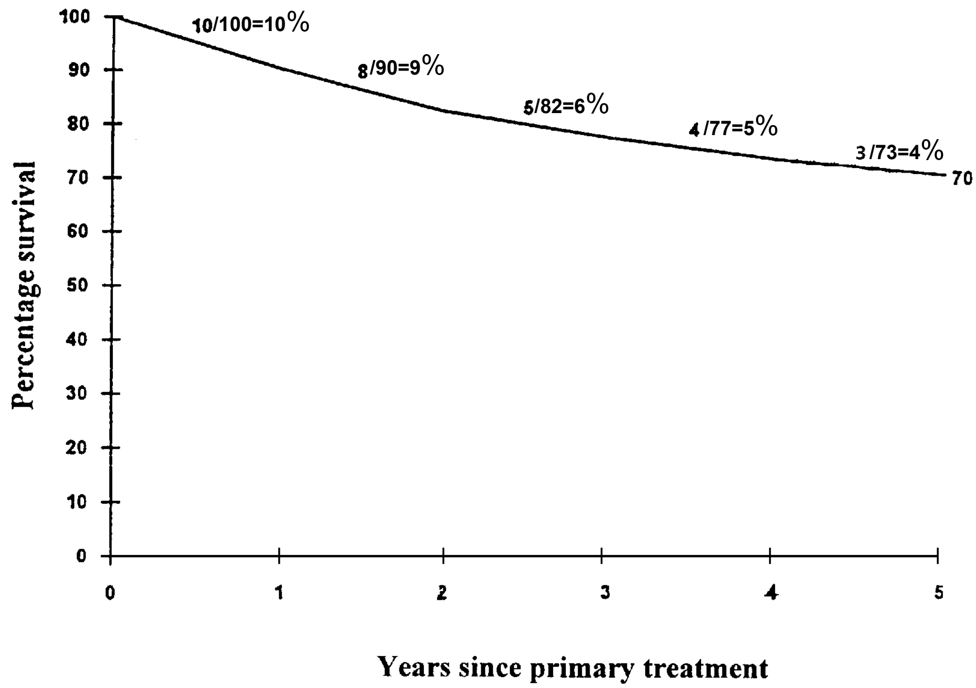

Figure 1: Overall five year survival after primary treatment for tumour X.

The graph represents the recurrence rates for all cases of tumour X. **[**These**]** data however, include a large spectrum of recurrence rates from very low (early stage disease) to very high (late stage disease). **[**To illustrate the effect of different stages on prognosis it is assumed that tumour**]** X lesions can be divided into three types, or stages, based on the pathological examination of the resected specimen.**[ ]**

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Studies have shown that the prognosis following surgical treatment for tumour X is related positively with the stage of the tumour at operation. Thus the previous overall five year survival curve of tumour X can be broken down into three separate curves relating to the three separate stages as shown in **[Figure 2]**. As would be expected, the more advanced stage tumours (stage 2 and 3) have a worse prognosis than early lesions.

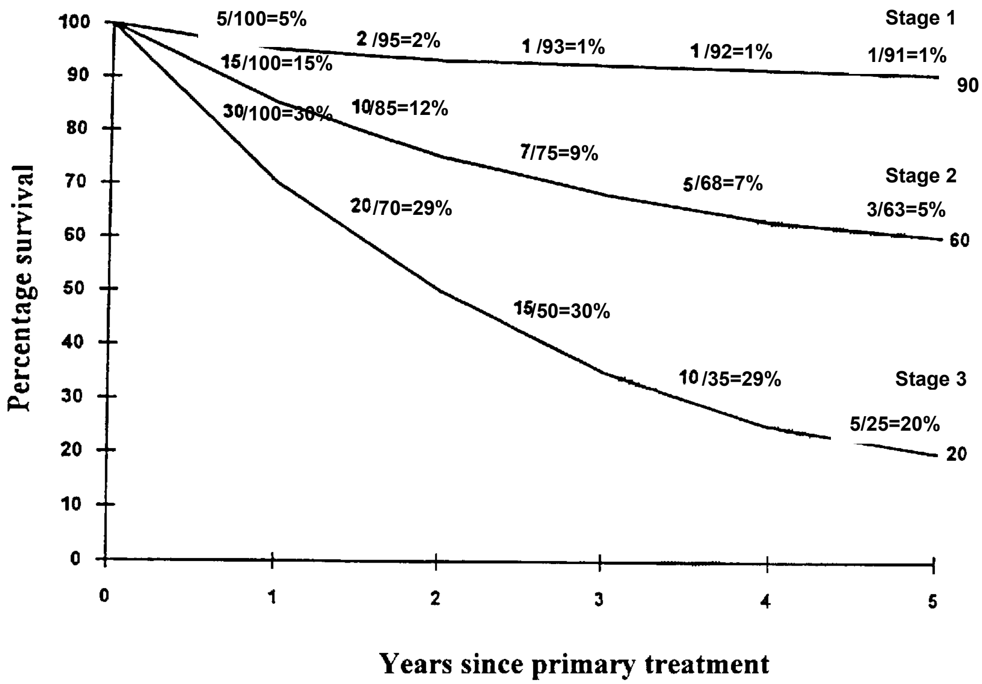

Figure 2: Five year survival for Tumour X divided into pathological stages

From the data in **[Figure 2]** it is possible to derive a yearly percentage risk of recurrence for any stage of tumour X. For instance, the risk of a recurrence between 2 and 3 years after surgery for a stage 2 tumour is **[**9 %**]**.

3.3 **Defining the site of recurrence**

Each tumour has its own particular sites of recurrence, and these have been recorded in pathology textbooks since **[**they**]** were first written. Although metastases can occur in any part of the body, the majority are found in the organs listed in **[**Table 3**]**.

[ ]

Site	Incidence
Local and lymph nodes	60%
Liver	20%
Lung	5%
Bone	5%
Bone marrow	0%
Brain	10%

Table [3**]: Incidence of metastasis by site**

[The percentage incidence figures in Table 3 are examples for the theoretical tumour X.**]** Ideally **[**these**]** data should relate to the incidence of a 'first recurrence' at these sites. This, however, is often difficult to find in the literature. Figures for the incidence of metastases in various organs at post-mortem is more easily obtained, and in some tumours an extrapolation from this data may be necessary to obtain a 'first recurrence' incidence.

3.4 **Defining the risk of a particular metastasis causing incapacitation**

A first recurrence in a regional lymph node carries a very small risk of incapacitation. A brain metastasis however, as the first indication of recurrent disease, **[**is assumed to**]** carry a 100% potential for sudden incapacitation in the form of a fit or seizure **[**or other neurological event such as paresis, sensory loss or headache**]**. Metastatic disease in bone marrow can cause anaemia and bleeding disorders. Rarely metastases may erode major vessels with catastrophic consequences (lung and liver). The risk of subtle incapacitation is harder to quantify, but it must be assumed that any recurrence of any tumour will degrade the operational abilities of air crew **[ ]** to some extent.

Thus a table of 'incapacitation weighting' can be constructed to give **[**an estimate**]** of the potential for sudden and subtle incapacitation by a recurrence at each metastatic site. This is shown in **[ ]** **[**Table 4**]**.

Site	Incapacitation 'weighting'	**[ ]**
Local and lymph nodes	5%	
Liver	5%	
Lung	5%	
Bone	5%	
Bone marrow	20%	
Brain	100%	

Table 4: Incapacitation weighting

3.5 **Defining the total risk of incapacitation**

Three parameters are now known about tumour X, and these can be used to **[**estimate**]** a 'total' risk of incapacitation. They are:

- The recurrence rate per year for any stage of tumour X (as a percentage).
- The frequency of metastatic disease in a particular organ (as a **[**percentage**]**).
- The risk that a metastasis in a particular organ will cause incapacitation (as a **[**percentage**]**).

A formula can now be derived to calculate the total risk of a particular metastasis causing incapacitation **[**in any year after completion of primary treatment**]**. The example below is for brain metastases.

Tumour X recurrence rate (%)	X	Incidence of brain metastases **(%)**	X	Risk of a brain metastasis causing incapacitation **(%)**	=	Incapacitation risk for brain metastases in tumour X **(%)**

Using the figures that we have obtained, numbers can be put to this formula. The tumour recurrence rates per year are from **Figure 2**.

Year 1 / Stage 1 : 5% X 10**[ ] %** X 100**[ ] %** = 0·5% risk of incapacitation

Year 1 / Stage 2 : 15% X 10**[ ] %** X 100**[ ] %** = 1·5% risk of incapacitation

Year 1 / Stage 3 : 30% X 10**[ ] %** X 100**[ ] %** = 3·0% risk of incapacitation

In the first year, therefore, the risk of incapacitation due to brain metastases ranges from 0.5% to 3.0%. This would allow a range of certification as shown in **[**Table 5**]**.

YEAR 1 – BRAIN METASTASES			
Stage	Incapacitation risk	Professional certification	Private certification
1	0·5%	'As or with copilot'	Unrestricted
2	1·5%	None	'Safety pilot'
3	3·0%	None	'Safety pilot'

Table 5: Range of certification possible in first year after completion of treatment

By year 5 the prognosis has improved and so have the incapacitation risks. Again the tumour recurrence rates are taken from **Figure 2**.

Year 5 / Stage 1 : 1 % X 10**[ ] %** X 100**[ ] %** = 0·1% risk of incapacitation

Year 5 / Stage 2 : **[** 5**]** % X 10**[ ] %** X 100**[ ] %** = **[**5**]** % risk of incapacitation

Year 5 / Stage 3 : **[**20**]** % X 10**[ ] %** X 100**[ ] %** = **[**2**]** % risk of incapacitation

In the fifth year the risk of incapacitation has now fallen to between 0·1 and **[**2**]** %. The range of certification has also improved, as shown in **[**Table 6**]**:

YEAR 5 – BRAIN METASTASES			
Stage	Incapacitation risk	Professional certification	Private certification
1	0.1%	Unrestricted	Unrestricted
2	0·5%	'As or with co-pilot'	Unrestricted
3	2%	None	"Safety Pilot"

Table 6: Range of certification possible in fifth year after completion of treatment

Obviously other types of recurrence are possible (and indeed more likely) than brain metastases, but because of the 'incapacitation weighting' given to each anatomical recurrence, brain lesions contribute most to the total risk of incapacitation. **[**The combined risks of several sites of recurrence may need to be taken into account**]**.

3.6 **Presenting the total risk of incapacitation**

[A table can be used to show the type of certification possible depending on time since completion of primary treatment and stage (Table 7):

Stage	Year since completion of primary treatment				
	1	**2**	**3**	**4**	**5**
1	0.5% (5%x10%x100%)	0.2% (2%x10%x100%)	0.1% (1%x10%x100%)	0.1% (1%x10%x100%)	0.1% (1%x10%x100%)
2	15%x10%x100% =1.5%	12%x10%x100% =1.2%	9%x10%x100% =0.9%	7%x10% x 100% =0.7%	5%x10%x100% =0.5%

Table 7: Certification possibilities according to stage and time since completion of treatment

This can be displayed graphically as in Figure 3:

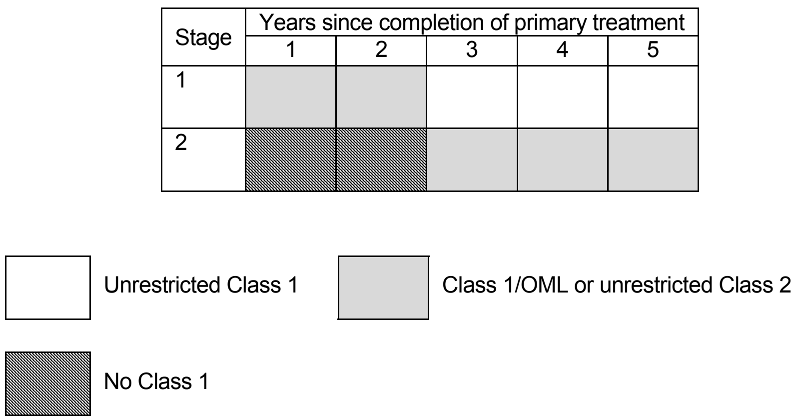

Figure 3: Bar chart representation of certification possibilities according to stage and time since completion of treatment]

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3.7 **Using certification assessment [charts]**

[It must be emphasised that charts are only for guidance and that aircrew with tumours that have a number of additional good prognostic factors may be returned to flying earlier than the 'average' example demonstrated by the chart. Conversely if adverse prognostic factors are present there may be a further delay before recertification.

The charts are based on published survival statistics following treatment for a particular type of tumour and may need revision if new therapy is introduced or the results of new studies become available. States can develop their own charts as guidance for the more common tumours based on the local prognostic factors and treatments used. Studies used to calculate the certification assessment figures may use overall, event-free or disease-free survival, and may include subjects unrepresentative of a pilot population (in terms of age, sex, country of residence, lifestyle and other variables) and may include cases where curative treatment has not been attempted. Individual case assessment therefore remains paramount.

These charts are useful for tumours that have a prognosis that improves with time. Some malignancies have a long median survival time of 10 years or more but the rate of progression remains relatively constant with time. It may be possible to maintain certification in this situation provided the licence holder remains asymptomatic, is not on active treatment and is reviewed regularly.**]**

3.8 **Tumour Markers**

[The relapse or active progression of certain tumours may be effectively followed by measuring tumour markers. The most common example in pilots and controllers is adenocarcinoma of the prostate where levels of Prostate Specific Antigen (PSA) can be tracked over a period of time.

Analysis of the tumour marker is very useful in determining the risk of relapse for an individual and it is inappropriate to use a certification assessment chart where this alternative type of targeted risk assessment is possible.**]**

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