A Photodynamic Therapy Patient Survey

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Keywords:	Photodynamic Therapy, Patient Survey, PDT

A Photodynamic Therapy Patient Survey: real-life experience from two regional services

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Topical photodynamic therapy (PDT) is widely used for actinic keratoses (AK), Bowen's disease (BD) and superficial basal cell carcinoma (BCC), with a strong evidence-base regarding efficacy and high levels of patient satisfaction (1). The British Association of Dermatologists published standards for PDT service delivery to ensure appropriate clinical governance, training and practices (2). Topical PDT involves application of a photosensitiser pro-drug (5-aminolaevulinic acid or methylaminolevulinate) and subsequent visible light exposure, generally using red LED light (conventional PDT; cPDT) (1). This initiates PDT phototoxicity, usually resulting in discomfort, pain and inflammation (3). Daylight PDT (dPDT) is also increasingly used for AK with high levels of tolerance (4, 5, 6).

Other treatment options include topical 5-fluorouracil (5-FU), imiquimod, ingenol mebutate (now discontinued), cryotherapy and surgery (1). Efficacy and adverse effects must be taken into account and patient and lesion characteristics, availability of services and patient choice typically influence treatment choice.

Historically, approximately 20% of patients reported severe pain with hospital-based PDT (3). However, our clinical impression was that over time as PDT services evolved, therapeutic tolerance has improved and pain rarely limits treatment delivery. Thus, we were keen to evaluate the real-life experience of patients receiving routine PDT in clinical practice outwith clinical trials, in two hospital settings. We evaluated this through a questionnaire-based approach.

The objectives of this survey were to evaluate the opinions of patients attending routine PDT clinics; specifically their views on PDT and other treatments received and to determine pain experienced during PDT. The questionnaires were developed by the authors and were in concordance with local hospital governance (Appendix: Supplementary information) and the survey was undertaken prospectively. Questionnaires were distributed in 2017 to patients attending one of two PDT clinics (Ninewells hospital (NWH), Dundee over 12 months and Queen Mary's Hospital (QMH), Roehampton, London over eight months), either immediately after PDT or during three-monthly follow-up. Completed questionnaires were returned at the end of the clinic visit, with 49% and 45% response rate at QMH and NWH respectively. Formal statistical analysis was not undertaken as numbers in subgroups were low and it was felt inappropriate to over-analyse data from this observational pilot survey.

A total of 155 patients (101 QMH; 55 NWH; 145 cPDT; 10 dPDT) completed the questionnaire. The demographics of patients were similar between centres, with an overall median age of 74 (range 36 - 92) years (Table 1). Overall, males and females were equally represented, although all 10 treated with

dPDT were male. Most patients received cPDT for BCC (33.8%) or BD (30.3%), whereas dPDT was used for AK (Table 1).

The majority of patients rated cPDT experience as “excellent” (67.6%) or good (22.8%), with similarly high ratings for dPDT (Table 1). Most cPDT patients experienced either mild (55.9%) or no (27.6%) pain, with similar;ly high tolerance levels rated for those who had dPDT (Table 1). Most patients experienced had mild erythemal reactions, with only 11% of cPDT patients developing marked redness and most did not experience oedema or exudation. Information provided about treatment was deemed useful by 98.1% of patients and most were satisified with cPDT (140, 96.6%) and dPDT (9, 90%), with only a few who would not have cPDT (4, 2.8%) or dPDT (1, 10.0%) again (Table 1).
One hundred and fifty patients (96%) were satisfied with PDT and 98% with the PDT information provided, with 79% being happy to have PDT again if required. Most patients (115; 74%) had received other treatments prior to PDT (Figure 1). Of the 30 who had received 5-FU, 25 (83%) described PDT as the superior treatment, with two preferring 5-FU and three reporting no difference. Of the 15 who had previously received Imiquimod, 12 (80%) preferred PDT, one preferred Imiquimod and two reported no preference. Of the four who had previously received ingenol mebutate, two preferred PDT and two described the treatments as similar, although ingenol mebutate is now no longer available. Of the 26 patients who had received cryotherapy, 15 (58%) preferred PDT, eight (31%) preferred cryotherapy and three (12%) reported no preference. Of the 70 patients who had surgery previously, 45 (64%) preferred PDT, 5 (7%) preferred surgery and 20 (29%) reported no preference. Reasons given for treatment preferences included convenience, effectiveness and adverse effects.

Most patients (117; 74%) had received other treatments prior to PDT (Figure 1). Of the 30 patients who had received 5-FU, 23 (82.1%) and 2 (100%) considered cPDT and dPDT respectively to be superior. Of the 15 cPDT patients who had previously received imiquimod, 12 (80.0%) preferred cPDT. Of the four who had previously received ingenol mebutate, two preferred PDT. Of the 24 patients who had received cryotherapy, 14 (58.3%) preferred cPDT and 7 (29.2%) preferred cryotherapy. Of the 70 patients who had surgery previously, 44 (64.7%) preferred cPDT and 1 (50%) preferred dPDT (Figure 1). Reasons given for treatment preferences included convenience, effectiveness and adverse effects.

Study limitations included use of an unvalidated patient questionnaire. We did seek an informal opinion of a user-experience designer to ensure the questionnaire as patient-orientated by minimising use of medical jargon and to ensure succinctness to minimise respondent fatigue (4). The purpose of the survey was to capture real-life experience of PDT and our data are in keeping with published findings from other studies reporting on patient satisfaction with daylight PDT (4,5,6).

In summary, we have shown that PDT in routine clinical practice, is well tolerated by the majority of patients, with high levels of satisfaction and most reporting either no or minimal pain and this is for both hospital-LED-based PDT as well as daylight PDT. Additionally, when compared with other commonly used treatments, most patients preferred PDT. These findings support the clinical utility of dermatological PDT services for patients with dysplasia and superficial non-melanoma skin cancer.

References

1. Wong TH, Morton CA, Collier N, Haylett A, Ibbotson S, McKenna KE, et al. British Association of Dermatologists and British Photodermatology Group guidelines for topical photodynamic therapy 2018. Br J Dermatol. 2019; 180: 730–9.
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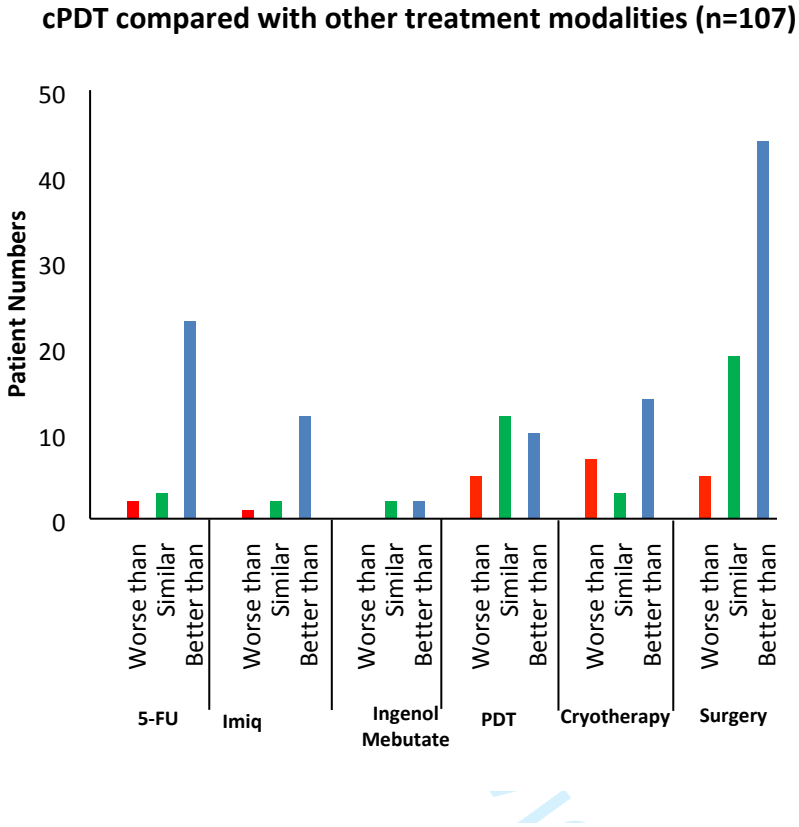
Legends

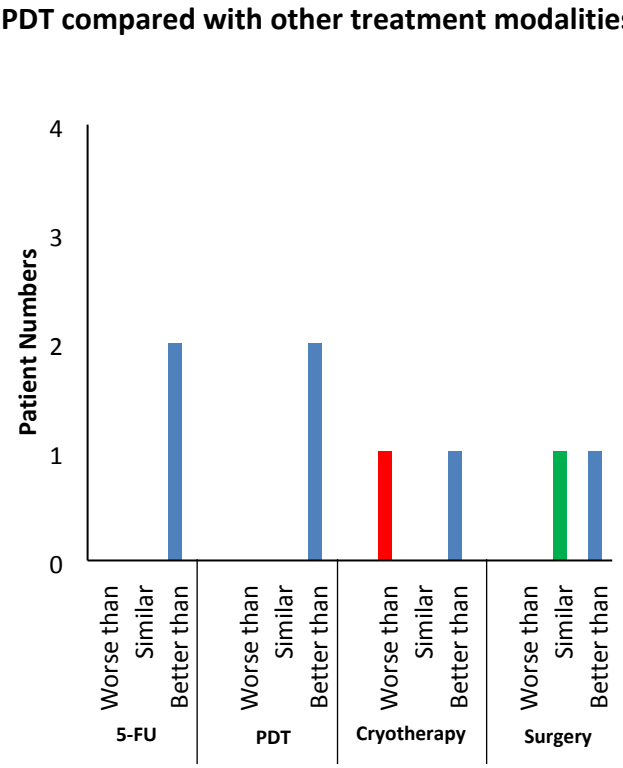
Appendix: Supplementary information – Questionnaire used in the PDT survey

Table 1: Demographics, disease characteristics, adverse effects and PDT treatment rating

Figure 1: Patient experience with previously used therapies

Figure 1


cPDT compared with other treatment modalities (n=107)
Patient Numbers
50
40
30
20
10
0
Worse than
Similar
Better than
5-FU
Imiq
Ingenol Mebutate
PDT
Cryotherapy
Surgery


dPDT compared with other treatment modalities (n=10)
Patient Numbers
4
3
2
1
0
Worse than
Similar
Better than
5-FU
PDT
Cryotherapy
Surgery

	cPDT		dPDT	
	n	%	n	%
Sex				
Male	57	39.3%	10	100.0%
Female	69	47.6%		
NR	19	13.1%		
Median Age	74		74	
Range	36-92		57-79	
Mean Age	74		70	
Std Deviation	12.6		11	
Diagnosis				
AK	17	11.8%	6	60.0%
Bowen's	44	30.3%		
sBCC	49	33.8%		
Multiple Diagnosis	10	6.9%		
Other	17	11.7%		
NR	8	5.5%	4	40.0%
Treatment Rating				
Excellent	98	67.6%	3	30.0%
Good	33	22.8%	3	30.0%
Fair	0	0.0%	1	10.0%
Poor	1	0.6%	0	0.0%
NR	13	9.0%	3	30.0%
Pain Rating				
No pain	40	27.6%	6	60.0%
Mild, annoying	81	55.9%	4	40.0%
Nagging, upsetting	15	10.3%	0	0.0%
Distressing, miserable	2	1.4%	0	0.0%
Intense, dreadful	5	3.4%	0	0.0%
Worst possible	1	0.7%	0	0.0%
NR	1	0.7%	0	0.0%
Redness				
Not red	6	4.0%	2	20.0%
Slightly pink /slightly red	47	32.0%	6	60.0%
Pink /Red	62	43.0%	0	0.0%
Very Red	16	11.0%	0	0.0%
NR	14	10.0%	2	20.0%
Swelling				
Yes	37	25.5%	0	0.0%
No	105	72.4%	8	80.0%
NR	3	2.1%	2	20.0%
Weeping				
Yes	30	20.7%	0	0.0%
No	109	75.2%	8	80.0%
NR	6	4.1%	2	20.0%
Leaflets Useful				
Yes	142	97.9%	10	100.0%
No	3	2.1%	0	0.0%
NR	0	0.0%	0	0.0%
Satisfied?				
Yes	140	96.6%	9	90.0%
No	0	0.0%	0	0.0%
NR	5	3.4%	1	10.0%
Therapy Again?				
Yes	117	80.7%	6	60.0%
No	4	2.8%	1	10.0%
NR	24	16.5%	3	30.0%

Photodynamic Therapy (PDT) Survey			Date:	
Age:		Sex: F / M	Diagnosis:	
Post Treatment ☐			Follow-up ☐	
Which treatment did you have?				
☐ Conventional PDT	☐ Daylight PDT	☐ Ambulatory PDT (Home-based)		
How do you rate the therapy overall?				
Excellent	Good	Fair	Poor	

Directly after therapy, rate the following:						
Pain:	 No pain	 Mild, annoying pain	 Nagging, upsetting pain	 Distressing, miserable pain	 Intense, dreadful, horrible pain	 Worst possible, unbearable pain
Redness:	Not red at all	Slightly pink	Pink	Slightly red	Red	Very Red
Swelling:	No			Yes		
Weeping:	No			Yes		

General questions about PDT session:		
How long did it take to travel to hospital? (including your wait for transport)		
How long did it take you to recover after therapy? *(for follow-up patients only)*		
Were the written leaflets useful and clear?	No	Yes
Were you satisfied with your therapy?	No	Yes
Will you have this therapy again?	No	Yes

1. Have you had any treatment before today for your lesions? Yes/No. (if "no" go to section 4)				
2. Compared to the treatment you had, how did this PDT treatment compare to the following?				
3. 5FU (Efudix)	Does not apply to me	Worse than 5FU	Similar to 5FU	Better than 5FU
Why worse or better?				
Imiquimod (Aldara)	Does not apply to me	Worse than imiquimod	Similar to imiquimod	Better than imiquimod
Why worse or better?				
Ingenol Mebutate (Picato)	Does not apply to me	Worse than Picato	Similar to Picato	Better than Picato
Why worse or better?				
PDT – *(please circle)* hospital-based/ ambulatory/Daylight PDT	Does not apply to me	Worse than previous PDT	Similar to previous PDT	Better than previous PDT
Why worse or better?				
Cryotherapy	Does not apply to me	Worse than cryotherapy	Similar to cryotherapy	Better than cryotherapy
Why worse or better?				

Surgery (include cut out or scraped off)	Does not apply to me	Worse than surgery	Similar to surgery	Better than surgery
Why worse or better?				
Other: _____	Does not apply to me	Worse than this	Similar to this	Better than this
Why worse or better?				

4. Is there anything else we should know? (i.e. general feedback, comfort, etc.)

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A total of 15~~56~~ patients (101 QMH; 55 NWH; 145 cPDT; 10 dPDT) completed the questionnaire~~.~~. The demographics of patients were similar between centres, with an overall median age of 7~~42~~ (range 36 - 92) years (Table 1). O~~There was a slightly higher male to female ratio in QMH (1.3 : 1), although~~

~~o~~verall, ~~-~~males and females were equally represented, although all 10 treated with dPDT were male. Most patients ~~had~~ received ~~treatment~~ cPDT for BCC (33.8%)~~D~~ or BD (30.3%)~~CC~~, whereas dPDT was used for AK ~~with others having AK or a combination of AK, BD, BCC. Most patients received hospital-based LED PDT, although 10 received daylight PDT and these data are presented separately as are those for lesion type~~ (Table 1).

The majority of ppatients ~~(102; 65%)~~ ratedeported ~~the~~ cPDT experience ~~overall~~ as "excellent" (67.6%) or good (~~and~~ 22.8~~3~~%), with similarly high ratings for dPDT (Table 1) ~~as "good"~~. Most cPDT patients experienced either mild (55.9%) or no (27.6%) pain, with similar;ly high tolerance levels rated for those who had dPDT (Table 1)~~Forty-seven patients (30%) reported that they experienced "no pain" and a further 85 patients (55%) reported "mild, annoying" pain; with the remaining 23 patients (15%) reporting more intense pain~~. Most patients experienced had mild erythemal reactions, with only 11% of cPDT patients developing marked redness ~~but no oedema or exudation~~and most did not experience oedema or exudation. Information provided about treatment was deemed useful by 98.1% of patients and most were satisfied with cPDT (140, 96.6%) and dPDT (9, 90%), with only a few who would not have cPDT (4, 2.8%) or dPDT (1, 10.0%) again (Table 1).

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other commonly used treatments, most patients preferred PDT. These findings support the clinical utility of dermatological PDT services for patients with dysplasia and superficial non-melanoma skin cancer.

References:

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Legends

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Figure 1: Patient experience with previously used therapies

November 2020

Professor Akimichi Morita
Editor-in-Chief
Professor and Chairman
Department of Dermatology
Nagoya City University,
Nagoya
Japan

Dear Professor Morita

Photodermatology Photoimmunology Photomedicine
PHOTO-LE-04-20-0338

Thank you for the most helpful feedback from yourself, Professor Leone and the two reviewers and we welcome the opportunity to have improved on this manuscript in the light of this feedback. We have addressed all comments and hope that the revised manuscript is now suitable for publication in Photodermatology Photoimmunology Photomedicine. We detail below the point by point response to feedback and include a revised manuscript with changes included and highlighted, along with a clean version of this revised manuscript.

Associate Editors comments
As indicated in the points below, we have included more details on methodology in paragraph 4, separated out the data in Table 1 to show conventional and daylight data separately and to highlight the different lesion types. We have also included in the text the questionnaire response rate at each of the two centres (Line 8 paragraph 4).

Reviewer: 1
Thank you for the positive feedback. We have corrected the typographical error on page 2, line 3 of reference 3: change "approacvh" to "approach".

Reviewer: 2

1. **I recommend presenting the results separated by the type of lesion treated making statistical analysis. In addition, the comparison with other treatments should be performed depending on the type of lesion. Also, daylight PDT and conventional PDT should be considered separately. A table is needed to present all these results.**

   We hope that revision to the text of paragraphs 5,6 and 7 and changes to Table 1 now addresses these points. In the last sentence of paragraph 4 we have now explained why formal statistical analysis was not undertaken in this small observational survey as we consider that over analysis of small subgroups could potentially be misleading.

2. **It is true that there is not a validated questionnaire specifically designed to evaluate patient's preference/satisfaction with PDT. However, there are previous studies with similar aims that the author should have taken into account in order to compare their results (See JA, et al. Dermatol Ther 2017;7:525; Garcia-Malinis A, et al. Eur J Dermatol 2018;28:113-115; Fargnoli MC et al. J Eur Acad Dermatol Venereol 2018;32:757-762).**

   Thank you and we have now included and referred to these three additional references in last lines of paragraphs 1 and 8 and include as references 4,5,6.

3. **The questionnaire used should be provided at least as supplementary material.**

   The questionnaire is now submitted as supplementary material and referred to in line 4 of paragraph 4.

4. **The methodology is quite poor. Please give the type of study, the period of time during the study was carried out, calculation of the sample size and the statistical analysis performed. If the questionnaire was done during the follow-up, what was the limit of time since the PDT was performed? I think it is important in order to consider memory bias.**

   We have now included more methodological information in paragraph 4, which explains how this prospective observational survey was undertaken and the follow up interval.

5. **156 patients completed the questionnaire. How many patients were requested to fill it? This data will tell us the percentage of response.**

   We have included the questionnaire response figures for each centre in line 8, paragraph 4.

6. **Besides the range of the age, it is useful either to give the standard deviation or the percentile 25-75 distribution in order to have an idea of the age distribution of the sample. A table summarizing the characteristics of the sample including sex, disease treated, type of treatment, photosensitizer used (MAL or ALA), type of PDT.**

   These data are now included in Table 1.

7. **The authors did not compare their results with others previously published; although they are not exactly the same because these studies focus only in actinic keratoses, and some only in daylight (See JA, et al. Dermatol Ther 2017;7:525; Garcia-Malinis A, et al. Eur J Dermatol 2018;28:113-115; Fargnoli MC et al. J Eur Acad Dermatol Venereol 2018;32:757-762)**

   Thank you and we have now included and referred to these three additional references in last lines of paragraphs 1 and 8 and include as references 4,5,6.

We hope that with these revisions the manuscript is now suitable for publication in Photodermatology Photoimmunology Photomedicine and we look forward to hearing from you.

Many thanks

Kind regards

Bernard Ho