CHAPTER 6

SCREDENT, a system for dental decision support in patients with head and neck cancer

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Submitted

Abstract

Objectives

To construct and test a computer-based system for dental decision support in patients with head and neck cancer.

Methods

Findings from our previous studies concerning pretherapy dental decision-making in patients with head and neck cancer were used to develop and test SCREDENT, a decision support system. Dental health status, radiotherapy conditions, and tooth loss in a sample of 209 patients were modeled in an iterative approach, using the aiNet-software, a probabilistic neural network application. ROC curve analysis, measures of accuracy, and logistic regression analysis were used to assess SCREDENT's performance in predicting tooth loss/ tooth extraction.

Results

Modelling and prediction procedures of the aiNet software were relatively simple and rapid. In all training, testing, and validation sequences, SCREDENT was able to reach a solution. Altogether, approximately 1660 vectors (representing teeth under examination) were processed. The results show that in almost 95% of the cases, SCREDENT's predictions for tooth extraction (conditional probability cut-off value: 0.5) agree with the actual tooth extractions carried out as part of the preradiation oral screening.

Conclusions

SCREDENT accurately predicts whether tooth extraction is the most favorable option for preradiation intervention. By means of feeding all appropriate decisions made on the basis of SCREDENT's predictions back into the training set, this system offers a framework for continuous updating and adjusting of the decisions process and therefore not only allows evidence-based decision-making, but also may be a component of a quality control system. A further attractive feature of SCREDENT may be its use for training inexperienced clinicians.

Introduction

High-dose radiotherapy to the head and neck, which includes oral and maxillofacial structures and salivary glands, may result in serious side effects. The short-term effects are mucositis, loss of taste and smell, secondary or "opportunistic" infections, and reduced salivary function. The long-term effects include persistence of reduced salivary function, radiation caries (Fig 6.1), progression of pre-existing periodontal disease activity, limited mouth opening (trismus), soft-tissue breakdown and failure to heal, and radiation bone injury, which in its severest form develops as osteoradionecrosis. As a secondary effect, patients with head and neck cancer experience significant tooth loss, prior to and following radiotherapy.(1,2)

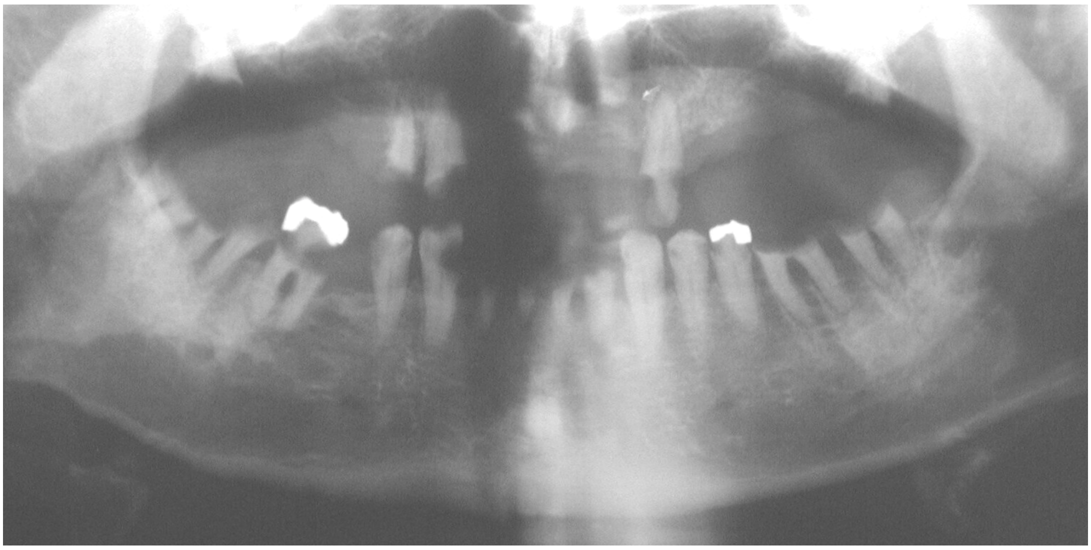


Figure 6.1 Orthopantomogram showing massive radiation caries, two years after radiotherapy for an oropharyngeal squamous cell carcinoma. Note the circumferential spread of the lesions, which resulted in amputation of clinical crowns.

To reduce oral sequelae of head and neck cancer therapy, extensive dental preventive and treatment measures before, during, and after cancer therapy are mandatory. (1,3-5) Implicit in the preventive approach is pretherapy oral screening to identify and eliminate dental risk factors for oral complications.(4) The current standards for dental care before radiation therapy include extraction of those teeth with significant bone loss, extensive caries, and/or extensive periapical lesions. In addition, partially impacted or incompletely erupted teeth and residual root tips not fully covered by bone and/or showing radiolucency to x-rays should be removed.(2,4,6-8)

Important factors in the dental management include, among others, the following considerations.[2,5,9]

(1) anticipated radiation field and dose;

(2) pretherapy dental status, dental hygiene, and retention of teeth that will be exposed to high-dose irradiation;

(3) patient's motivation and ability to comply with preventive measures.

Although several studies strongly support the efficacy of the pretherapy oral screening,[6,10,11] evidence-based clinical guidelines[12-14] to aid clinicians in deciding which options for dental intervention suit these patients best are not yet widely available. In view of the risk that results from high-dose irradiation, special attention to preradiation dental planning appears critical.[2,5] Each case must be managed individually; a single-formula approach for all patients is contra-indicated.[2] The key to control may be the implementation of a dental decision support system, derived from an evidence-based approach.

Evidence-based medicine is an approach to clinical judgment and decision-making in which the clinician uses the best evidence available to decide upon the intervention that suits an individual patient best.[15] This approach involves the rigorous evaluation of the effectiveness of health-care interventions, dissemination of the results of evaluation, and application of these findings toward improvement of clinical practice.[16] Good clinicians use both individual clinical expertise and the best available external evidence, and neither alone is enough. External clinical evidence can inform but can never replace individual expertise. Evidence-based medicine is therefore not an obligatory "cookbook" approach.[17]

This survey forms part of an international research project on dental decision support in patients with head and neck cancer.[5,9,18] The aim of the current survey was to construct and test a system to support dental decision-making, prior to radiotherapy for head and neck cancer. We first summarize some characteristics of decision support systems. We then propose "SCREDENT," a system for dental decision support in head and neck cancer patients.

Decision support systems are interactive, computer-based systems that aid users in judgment and decision-making. They provide data storage and retrieval and support framing, modeling, and problem solving, as depicted in Fig 6.2. Decision support systems are especially valuable in situations in which confidence and reliability are of importance. There are several types of decision support system, such as belief networks, influence diagrams, probabilistic expert systems, and artificial neural network applications.[19] We used a software package to emulate a neural network[20] as formal constructional technique for SCREDENT.

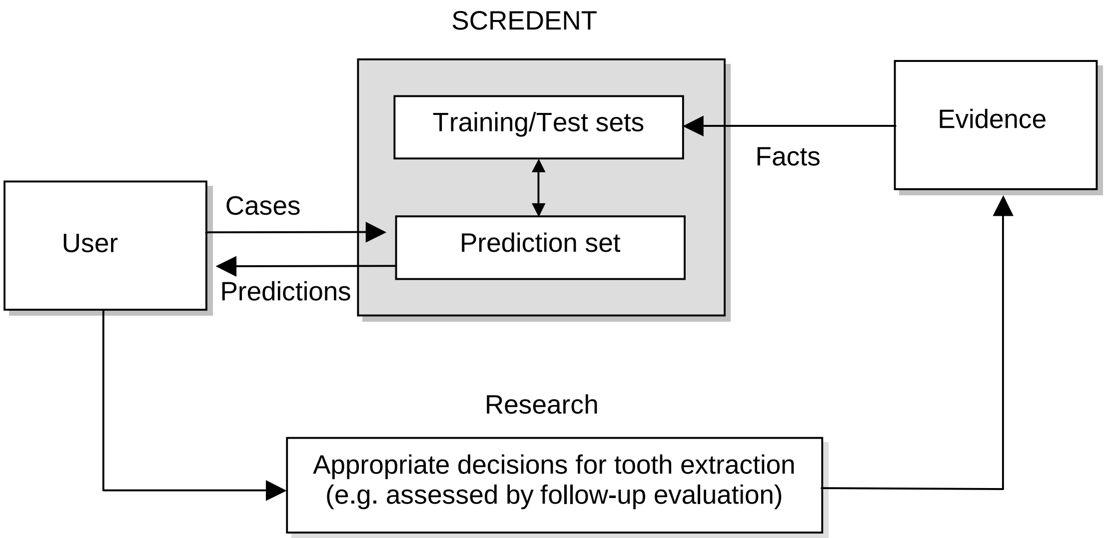


Figure 6.2 Diagram of SCREDENT, a computer-based decision-support system. The gray box represents the part of SCREDENT that is modeled using the probabilistic neural network (aiNet software). The predictions from SCREDENT are conditional probabilities for tooth loss/ tooth extraction. All decisions for tooth extraction that proved to be appropriate should be re-entered into SCREDENT's training set, assuring an evidence-based approach.

The potential benefits of neural-network software seem obvious to those who design them but are often less clear to the end user.(21) Many clinicians are suspicious of these network applications and look upon them as "black boxes". The benefits of analyses using neural networks over more conventional methods, especially for analysis of complex and noisy data, must therefore be clearly demonstrated. In addition, according to Cross et al.,(21) useful software applications must be, among others things, robust and easy to use. While the quality and reliability of decision support systems are important, the most crucial aspect is their user interface. Systems with cumbersome or unclear user-interfaces are rarely useful.

Artificial neural networks have been extensively studied and applied.(20,22-25) This has resulted in numerous research reports in this area. The most common neural-network learning algorithm in biomedical applications is "back-propagation" in "multilayer perceptrons."(26) We used a type of neural network with a different architecture, the Probabilistic Neural Network (PNN). This type of neural network acts as a classifier or predictor that overcomes many of the problems of back-propagation. It has self-organizing properties(27) and trains virtually instantaneously. At present, although there have been relatively few applications of PNN modelling in biomedical situations, all have performed well.(28) Readers looking for more information on neural networks are referred to comprehensive introductory texts.(20,21,29-37)

Materials and methods

The subjects came from a previous clinical study, conducted in 1999.[18] These patients (n=209) had undergone head and neck cancer therapy at the Otorhino-laryngology department and allied departments of University Medical Center Utrecht, The Netherlands, between 1993 and 1998. Patients selected for inclusion in that clinical survey were required to satisfy the following conditions: they (1) were in the regular cancer follow-up schedule; (2) had undergone primary cancer treatment, including radiation therapy, for squamous cell carcinoma in head and neck, one to five years previously; (3) were treated with the intention of curing the disease (patients receiving only palliative treatment or patients with active disease were not included for ethical reasons); and (4) had undergone preradiation dental screening. A second, more recent patient sample was analyzed in order to further validate SCREDENT. This sample consisted of 30 patients who were treated in the University Medical Center Utrecht in the year 2000. Informed consent was acquired from the patients who were found to meet the criteria for inclusion in the study protocol.

Data on dental health status and tooth loss were obtained via pretherapy oral screening. We used a specially designed dentition assessment form- the SCREDENT form- that together with comprehensive instructions and a "getting started" document, is available for download from the Internet.[1] The "SCREDENT, getting started" document also presents an example of a clinical case, illustrating how the findings from the preradiation oral screening should be recoded and entered into SCREDENT in order to make predictions for tooth extraction.

The SCREDENT data collection form was designed and tested using the results from our previous studies. Among other variables, such as type, location, and stage of head and neck tumor, the following, fully described in the SCREDENT instruction document, were recorded:

Input variables:

(1) "*dmftot*": the number of teeth retained
(2) "*drftot*": the total number of high Dental Risk Factors[5]
(3) "*upper*" / "*lower*": the location of the tooth
(4): "*molar*" / "*bicusp*" / "*cusp*" / "*incis*": the type of tooth
(5) "*gland*": major salivary glands in high-dose irradiation field
(6) "*trx*": tooth in high-dose radiation field
(7) "*patfact*": patient's dental IQ

Output variable:

(8) "*tloss*" : tooth extraction/ tooth loss

Using these eight variables, the decision problem analyzed in this paper was modeled graphically, as depicted in Fig 6.3. The solid arrows indicate the correlations between variables which were the scope of the present study. The dotted arrows indicate correlations that are present but were not further specified.

[1] Available for download at the Internet at http://www.mexsys.net. *(See also Appendices 2,3.)*

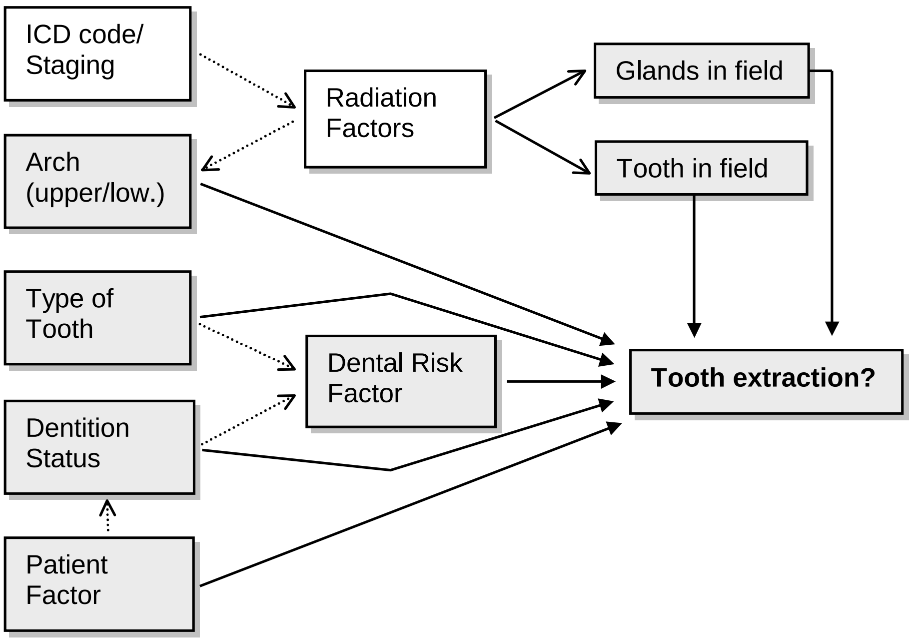
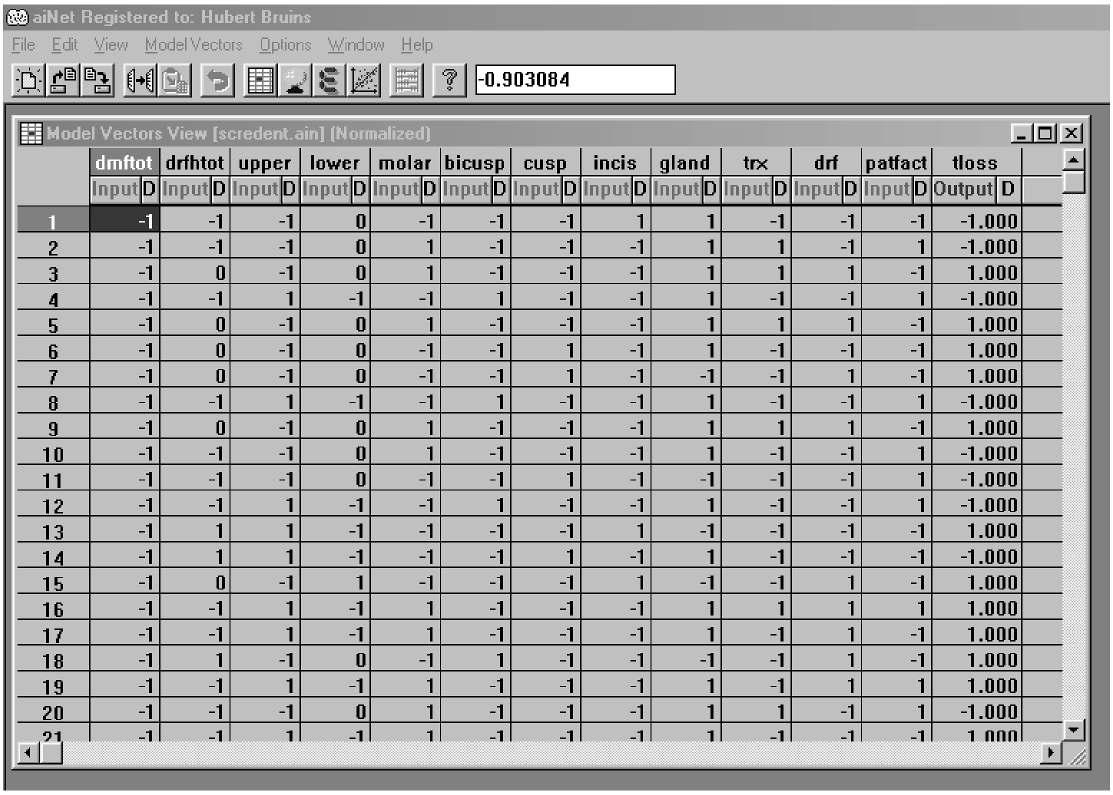


Figure 6.3 Schematic representation of the variables involved in the decision problem. The solid arrows indicate the correlations between the variables that are modeled using aiNet software.
(*ICD code*: International Classification of Diseases, Ninth Revision, Clinical Modification, as published by the U.S. Public Health Service and Health Care Financing Administration)

The next phase of the analysis was the neural-network computing. We used the aiNet software package (aiNet for Windows, version 1.25, aiNet, Celje, Slovenia) to run the PNN on a personal computer.[2] All sets of eight variables, including the known output variables ("*tloss*") were recoded into 2 discrete and 11 binary variables. This process resulted in sets of 13 variables, the so-called "training vectors." aiNet has a spreadsheet-type interface, depicted in Fig 6.4, to enter and store the "training set." The procedure of modeling, data encoding, and data entering is thoroughly described and illustrated with examples in aiNet's manual and in the "SCREDENT, getting started" document. Interested readers are invited to download the SCREDENT files in order to try out the system.

[2] A full working version of aiNet (version 1.25), including online help files, examples, and a comprehensive manual in Microsoft Word format (Microsoft Corporation, Redmond, Washington, WA), can be obtained through download from the Internet. (http://www.ainet-sp.si/NNdownload.htm).



	dmftot	drfhtot	upper	lower	molar	bicusp	cusp	incis	gland	trx	drf	patfact	tloss
	Input D	Input D	Input D	Input D	Input D	Input D	Input D	Input D	Input D	Input D	Input D	Input D	Output D
1	-1	-1	-1	0	-1	-1	-1	1	1	-1	-1	-1	-1.000
2	-1	-1	-1	0	1	-1	-1	-1	1	1	-1	1	-1.000
3	-1	0	-1	0	1	-1	-1	-1	1	1	1	-1	1.000
4	-1	-1	1	-1	-1	1	-1	-1	1	-1	-1	1	-1.000
5	-1	0	-1	0	1	-1	-1	-1	1	1	1	-1	1.000
6	-1	0	-1	0	-1	-1	1	-1	1	-1	-1	-1	1.000
7	-1	0	-1	0	-1	-1	1	-1	-1	-1	1	-1	1.000
8	-1	-1	1	-1	-1	1	-1	-1	1	-1	-1	1	-1.000
9	-1	0	-1	0	1	-1	-1	-1	1	1	1	-1	1.000
10	-1	-1	-1	0	1	-1	-1	-1	1	-1	-1	1	-1.000
11	-1	-1	-1	0	-1	-1	1	-1	-1	-1	-1	1	-1.000
12	-1	-1	1	-1	-1	1	-1	-1	1	-1	-1	1	-1.000
13	-1	1	1	-1	-1	-1	-1	1	-1	-1	-1	-1	1.000
14	-1	1	1	-1	-1	-1	1	-1	1	-1	-1	-1	-1.000
15	-1	0	-1	1	-1	-1	-1	1	-1	-1	1	-1	1.000
16	-1	-1	1	-1	1	-1	-1	-1	1	1	1	1	1.000
17	-1	-1	1	-1	1	-1	-1	-1	1	-1	1	-1	1.000
18	-1	1	-1	0	-1	1	-1	-1	-1	-1	1	-1	1.000
19	-1	-1	1	-1	1	-1	-1	-1	1	-1	1	1	1.000
20	-1	-1	-1	0	1	-1	-1	-1	1	1	-1	1	-1.000
21	-1	-1	1	-1	1	-1	-1	-1	1	-1	-1	-1	1.000

Figure 6.4 aiNet's model vector view illustrating the first 20 model vectors of SCREDENT's training set (approximately 1660 model vectors).

To test SCREDENT's performance, six separate samples of 60 training vectors (test sets) were randomly retracted from the training set and used to make predictions. The values of the known output variable ("*tloss*") were deleted, so these samples consisted of only the 12 input variables. Each row comprising the 12 input variables with the missing output variable is called a "test vector." Running aiNet's prediction option, the missing output variable ("*tloss*") of each test vector was predicted on the basis of the data in the training set. The prediction is given as the conditional probability that the tooth under examination should be extracted or will be lost. The value of this conditional probability lies between 0 (no tooth extraction) and 1 (tooth extraction). Next, these predictions were compared to the actual output variables, the tooth extractions that were or were not carried out as part of the pretherapy dental screening. Receiver Operating Characteristic (ROC) curve analysis, described in detail elsewhere,[38-40] was used to assess SCREDENT's performance. In addition, true-positive, true-negative, false-positive, and false negative values and "overall accuracy" were computed. Overall accuracy is defined as true positives plus true negatives divided by total sample size. In addition, we compared SCREDENT's performance to logistic regression analysis, using the aggregation of test sample 1-6. This aggregated sample is designated "test sample 7" (see Table 6.1).

To further validate the model, a validation set consisting of the second patient sample was used to repeat SCREDENT's predictive accuracy. Again, a ROC analysis was carried out and accuracy was assessed.

Results

Modeling and prediction procedures of the aiNet software were relatively simple and rapid. In all training, testing, and validation sequences, SCREDENT was able to arrive at a solution. Altogether, approximately 1600 vectors (representing teeth under examination) were processed.

Table 6.1 Summary of SCREDENT test samples

SCREDENT Sample	*True pos.*	*False pos.*	*True neg.*	*False neg.*	*Sensitivity*	*Specificity*	*Area under the ROC Curve*[1]	*Accuracy (%)*
test 1	9	1	47	3	0.75	0.97	0.967	93
test 2	17	3	39	1	0.89	0.98	0.979	93
test 3	17	5	36	2	0.89	0.87	0.945	88
test 4	17	4	34	5	0.77	0.89	0.941	85
test 5	13	0	45	2	0.86	1.00	0.987	97
test 6	21	2	34	3	0.87	0.94	0.970	92
Validation n = 417	185	6	213	13	0.93	0.97	0.987	95
Overall n = 777	279	21	448	29	0.90	0.95	0.968	94
SCREDENT test 7	94	14	236	16	0.85	0.94	0.955	92
Logistic regression test 7	85	10	240	25	0.77	0.96	0.953	90

[1] Area under the ROC curves: asymptotic significance level, $p < 0.001$

The results show that in almost 95% of the cases, SCREDENT's predictions for tooth extraction (conditional probability cut-off value: 0.5) agree with the actual tooth extractions carried out as part of the preradiation oral screening. True-positive, true-negative, false-positive, and false negative values are shown in Table 6.1, along with sensitivity and specificity values. Fig 6.5 displays ROC curves. The areas under the ROC curves of the test samples ranged from 0.941 to 0.987 (mean 0.964), which also demonstrates a very high predictive accuracy. The area under the ROC curve of the validation sample was 0.987, which was the second highest of all ROC curves. It should be noted here that SCREDENT's specificity is slightly better than its sensitivity. This means that SCREDENT predictions are more accurate when a tooth should not be extracted or will not be lost than when a tooth requires extraction.

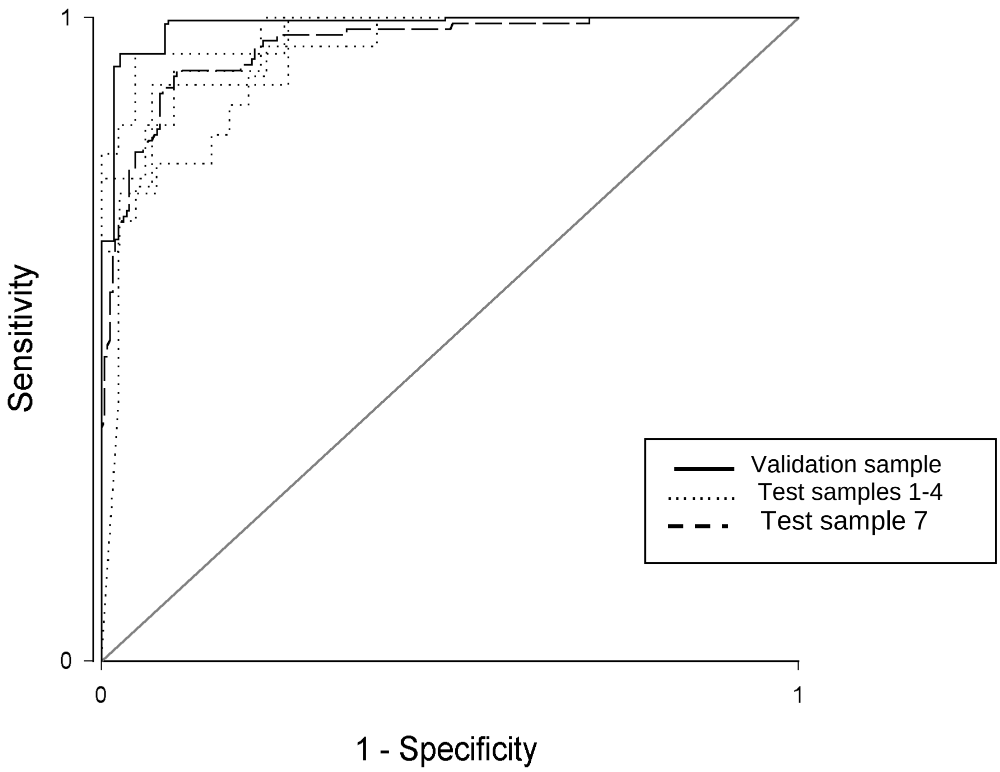
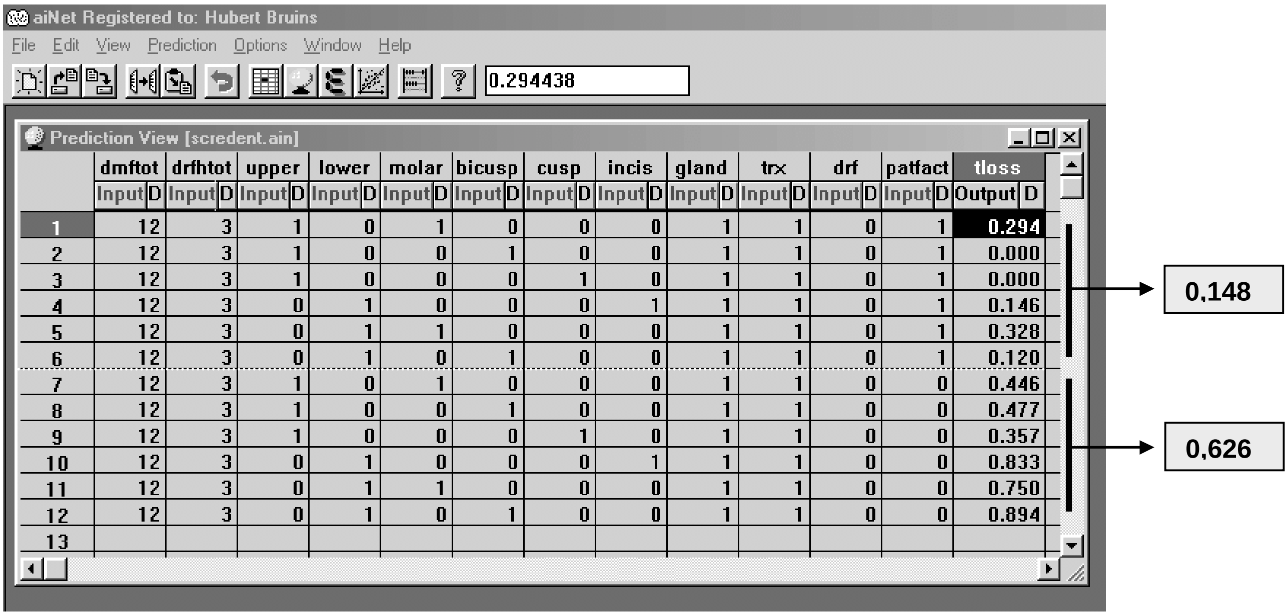


Figure 6.5 Receiver Operating Characteristics (ROC) curves.

SCREDENT predictions revealed that the patient factor "*patfact*" has a major influence on the prediction values. A hypothetical prediction example is depicted in Fig 6.6. The output values (conditional probabilities) in the column "*tloss*" were predicted on the basis of the model vectors in the training set with known outputs. Rows 1-6 represent teeth (together with dental health status and radiotherapy conditions) of a patient with a high 'dental IQ' (*patfact*=1). The overall 'mean' conditional probability for tooth loss (dental extraction) is 0,148. Rows 7-12 represent the same teeth, but now for a patient with unfavorable "dental IQ" (*patfact*=0). The overall "mean" conditional probability for tooth loss is now 0.626, that is 4.2 times higher, which shows that the mean probability of tooth loss (column "*tloss*") in patients with "*patfact*" = 1 (high dental IQ), in rows 1-6, is 4.2 times higher than in cases with "*patfact*" = 0 (average/low dental IQ), in rows 7-12.



	dmftot	drfhtot	upper	lower	molar	bicusp	cusp	incis	gland	trx	drf	patfact	tloss
	Input D	Input D	Input D	Input D	Input D	Input D	Input D	Input D	Input D	Input D	Input D	Input D	Output D
1	12	3	1	0	1	0	0	0	1	1	0	1	0.294
2	12	3	1	0	0	1	0	0	1	1	0	1	0.000
3	12	3	1	0	0	0	1	0	1	1	0	1	0.000
4	12	3	0	1	0	0	0	1	1	1	0	1	0.146
5	12	3	0	1	1	0	0	0	1	1	0	1	0.328
6	12	3	0	1	0	1	0	0	1	1	0	1	0.120
7	12	3	1	0	1	0	0	0	1	1	0	0	0.446
8	12	3	1	0	0	1	0	0	1	1	0	0	0.477
9	12	3	1	0	0	0	1	0	1	1	0	0	0.357
10	12	3	0	1	0	0	0	1	1	1	0	0	0.833
11	12	3	0	1	1	0	0	0	1	1	0	0	0.750
12	12	3	0	1	0	1	0	0	1	1	0	0	0.894
13													

Figure 6.6 SCREDENT's prediction view of a hypothetical sample, further explained in text

Discussion

Many clinical decisions are based primarily on values or beliefs and on various resources: opinion-based decision-making. At present, more and more attention is being given to evidence derived from research: evidence-based decision-making.[15,17] As stated before, good clinicians use both individual clinical expertise and the best available external evidence. In this paper, we propose SCREDENT, a system to support dental decision-making in patients with head and neck cancer. The rationale for constructing SCREDENT came from the understanding that decision-making in this area is often critical while evidence-based guidelines were not yet available.[5,9]

SCREDENT incorporates a patient factor, describing patient's "dental-mindedness" or "dental IQ,"[41] that significantly influences the outcome of the prediction. The patient factor stresses the importance of the patient's overall dental health at the time of the pretherapy dental screening, as noted in our previous study.[18] We have found that, when a head and neck cancer patient presents with poor dental health at the pretherapy oral screening, there will be substantial preradiation tooth loss. Moreover, if these patients have remaining teeth during irradiation, they are more likely to continue to develop dental pathosis following radiotherapy than are patients who present with satisfactory dental health.[42] Subsequent to the radiation, they will need extensive dental treatment, including tooth extractions. Consequently, the initial treatment planning, enhanced by SCREDENT, should include the anticipation that the remaining dentition of patients presenting with poor dental health may continue to deteriorate. In these cases, SCREDENT accurately predicts whether tooth extraction is the most favorable option for preradiation intervention.

Comparing SCREDENT's performance to the logistic regression model shows that SCREDENT performs slightly better (accuracy 92%, versus 90% for the logistic regression model). However, unlike the logistic regression model, SCREDENT can handle missing or inaccurate data,[22] and the explicit form of the relationships between the input variables and the output does not have to be specified in neural network models.[43]

A very important issue is to verify whether the predictions are applicable to the patient under examination. Additional considerations, such as the lack of clinical or financial resources, may require adjustment of the overall treatment plan. In addition, timing considerations are very important. If the interval between the preradiation oral screening and the start of the radiotherapy is limited, dental intervention involving extensive dental treatments is usually not possible. On the other hand, teeth requiring extraction, as indicated by SCREDENT, can be left in place until later if they are NOT in the high-dose radiation field. This demonstrates that a decision support system is not prescriptive. SCREDENT can inform, but it can never replace individual expertise.

The fact that the validation sample produced the second highest accuracy result may reveal a form of bias. Developing SCREDENT obviously provided feedback to the decision-making authors. Analysis of the decision problem yielded additional knowledge. In effect, it may have influenced the decision-makers' opinion and degree of belief in the appropriateness of the dental intervention decisions, leading to decisions that were more congruent with SCREDENT's predictions. This also illustrates the dynamic property of decision support systems.[27,32,44] By means of feeding all appropriate decisions made on the basis of SCREDENT's predictions back into the training set, a framework is created for continuous updating and adjusting of the decision process. This not only allows evidence-based decision-making but also may be a component of a quality control system. A further attractive feature of SCREDENT may be its use for training inexperienced clinicians.

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